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IN THE

Supreme Court of the United States

OCTOBER TERM, 1993

NORTH AMERICAN VACCINE, INC. and
NATIONAL RESEARCH COUNCIL OF CANADA,
Petitioners,

v.

AMERICAN CYANAMID COMPANY and
PRAXIS BIOLOGICS, INC.,
Respondents.

Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

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PETITION FOR A WRIT OF CERTIORARI

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QUESTION PRESENTED

Did the U.S. Court of Appeals for the Federal Circuit exceed its reviewing jurisdiction by invoking the harmless error doctrine on the basis of its independent determination of the fact-based meaning of technical terms in a patent claim, after holding that the District Court's findings related to that issue were infected with error?

PARTIES

The National Research Council of Canada is an agency corporation of Canada, wholly owned by Her Majesty the Queen in Right of Canada, reporting to Parliament through the Minister of Industry, Science and Technology. The parent companies, subsidiaries (except wholly-owned subsidiaries), and affiliates that have issued shares to the public, of North American Vaccine, Inc. are IVAX Corporation and BioChem Pharma, Inc.

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OPINIONS OF OTHER COURTS

The petitioner commenced this action in the U.S. District Court for the Southern District of New York. The Court's oral findings of fact and conclusions of law (App. at 28a-44a) are reported at 24 U.S.P.Q.2d 1898 (S.D.N.Y. 1992).

The majority (App. at 1a-17a) and dissenting (App. at 18a-26a) opinions of the U.S. Court of Appeals for the Federal Circuit, which affirm in part and reverse in part the District Court's judgment, are reported at 7 F.3d 1571 (Fed. Cir. 1993).

The Court of Appeals' order denying the petitioners' petition for rehearing and suggestion of rehearing in banc (App. at 45a-46a) is unreported.

JURISDICTION

The judgment of the U.S. Court of Appeals for the Federal Circuit was entered on October 6, 1993.

On October 27, 1993, the petitioners filed a timely petition for rehearing and suggestion of rehearing in banc, which the Court denied on December 8, 1993.

This Court has jurisdiction to review the judgment of the Court of Appeals under 28 U.S.C. § 1254(1).

STATUTORY PROVISIONS INVOLVED IN THE CASE

1. 28 U.S.C. § 2111 provides:

> § 2111. Harmless error
>
> On the hearing of any appeal or writ of certiorari in any case, the court shall give judgment after an examination of the record without regard to errors or defects which do not affect the substantial rights of the parties.

2. Rule 52(a) of the Federal Rules of Civil Procedure provides:

> Rule 52. Findings by the Court; Judgment on Partial Findings
>
> (a) Effect. In all actions tried upon the facts without a jury or with an advisory jury, the court shall find the facts specially and state separately its conclusions of law thereon, and judgment shall be entered pursuant to Rule 58; and in granting or refusing interlocutory injunctions the court shall similarly set forth the findings of fact and conclusions of law which constitute the grounds of its action. Requests for findings are not necessary for purposes of review. *Findings of fact, whether based on oral or documentary evidence, shall not be set aside unless clearly er-*

> *roneous, and due regard shall be given to the opportunity of the trial court to judge of the credibility of the witnesses.* The findings of a master, to the extent that the court adopts them, shall be considered as the findings of the court. It will be sufficient if the findings of fact and conclusions of law are stated orally and recorded in open court following the close of the evidence or appear in an opinion or memorandum of decision filed by the court. Findings of fact and conclusions of law are unnecessary on decisions of motions under Rule 12 or 56 or any other motion except as provided in subdivision (c) of this rule.

(Emphasis supplied.)

STATEMENT OF THE CASE

Introduction

This case involves the standard of review applied by the U.S. Court of Appeals for the Federal Circuit in determining that a patent held by the petitioners was not infringed. It raises an important question of the proper relationship between the Federal Circuit and the U.S. District Courts in deciding patent cases.

In the decision from which the petitioners seek a writ of certiorari, a panel of the Federal Circuit held that the District Court's decision was based on error, but nevertheless affirmed that decision under the harmless error doctrine by independently deciding factual questions based in part on selected trial testimony, in violation of Rule 52(a) of the Federal Rules of Civil Procedure. In so doing, the Federal Circuit undermined the District Court's role as fact finder to determine the credibility of witnesses.

The Petitioners' Patent

The petitioners are the owner and licensee of U.S. Patent No. 4,356,170 ("the patent"), issued to Harold J. Jennings and Czeslaw Lugowski. The technology em-

braced by the patent involves vaccines against bacterial infections such as meningitis, which can have devastating effects on young children. These vaccines employ "polysaccharides," which are components of bacteria that stimulate the human immune system to make antibodies. The patented invention is a vaccine made from "conjugates" (which are simply molecules chemically joined together), in which a protein is linked to a "terminal portion" or end of the polysaccharide.

The Respondents' Accused Product

The respondents' product accused of infringement is an infant meningitis vaccine called HibTITER. HibTITER is based upon a species of polysaccharide expressly recited in the asserted claims of the patent. The HibTITER vaccine contains some polysaccharides having a protein linked to only one terminal portion and others having proteins linked to both terminal portions.

The District Court Decision

Pursuant to 28 U.S.C. § 1338(a), the petitioners commenced this action in the U.S. District Court for the Southern District of New York, charging the respondents with infringement of the patent by the manufacture and sale of HibTITER. At trial, the parties presented "a substantial amount of testimony and documents received into evidence bearing on the question of interpretation" of the claims at issue. App. at 35a; 24 U.S.P.Q.2d at 1901.

Immediately following the parties' closing statements, the Court delivered oral findings of fact and conclusions of law. The Court stated: "I think the case is a close one" and "the scales tip, not drastically, but I think they tip in favor of the defense." App. at 29a; 24 U.S.P.Q.2d at 1898. The District Court found the pertinent claims of the patent invalid (a holding reversed by the Court of Appeals). The District Court, however, also made findings on the issue of infringement.

In its infringement analysis, the District Court was required to determine whether the phrase "linked . . . to a terminal portion of the polysaccharide" encompasses conjugates having proteins at both ends of the polysaccharide and not just one. Obviously, a conjugate having a protein at both ends can be said to be in the category of conjugates having a protein at an end. After concluding that the language, by itself, could be read either way, the Court proceeded to consider extrinsic evidence, including an article and a speech by Jennings, one of the inventors, concerning his research.

Based on a detailed analyses of the extrinsic evidence, the District Court held that the claims of the patent were limited to conjugates with a protein linked to only one terminal portion. In so holding, the Court stated that "the basic reason why I am holding in favor of the defendants on the question of interpretation" is that the patent did not clearly express "in the English language" either the inventor's intention "to broaden his patent beyond what was contained in the article and the speech" or his intention "to depart from the objectives that he so clearly had in his experimentation described in his article and his speech." App. at 39a; 24 U.S.P.Q.2d at 1902.

The Appeal

On appeal, a panel of the Federal Circuit unanimously reversed the District Court's holding of invalidity, but affirmed its holding of noninfringement by a divided vote.

In its opinion, the Court specifically rejected the District Court's reliance on Jennings' article and speech, stating that "[t]here is no inconsistency between writing a paper (or giving a speech) on a particular embodiment of an invention and then claiming one's invention more broadly in a patent application." App. at 13a; 7 F.3d at 1578. Thus, the Federal Circuit clearly held that the District Court had made a major error by concluding "that the narrow scope of the article limits the scope of the

patent claims, which should be judged on their own merits." *Id.*

Notwithstanding the closeness of the case and the District Court's improper reliance on the article and speech, the Federal Circuit did not remand the case to the District Court for reconsideration of the infringement issue on a proper standard and relevant evidence. Instead, a majority of the Federal Circuit panel found the District Court's error to be harmless by making its own independent *de novo* factual determinations in light of selected evidence in the record.

In dissent, Circuit Judge Rader stated:

> The panel's opinion correctly notes the trial court's error in relying extensively on the inventors' scientific articles for its claim interpretation. The trial court referred to the scientific writings as "the most important point in the evidence." Surprisingly, however, the panel's opinion did not consider this error a cause for reversal. In a case the district court repeatedly characterized as "very close," this extensive reliance on impermissible evidence constitutes reversible error. Without the primary source of evidence upon which the district court based its decision, this "very close" case would no doubt have ended differently.

App. at 18a; 7 F.3d at 1580 (Rader, J., dissenting).

REASONS FOR GRANTING THE WRIT

The U.S. Court of Appeals for the Federal Circuit has exclusive jurisdiction over appeals from all U.S. District Courts in patent cases. Because of this unique nationwide jurisdiction, this Court has stated that the Federal Circuit's appellate role is "a matter of special importance to the entire Nation." *Cardinal Chem. Co.* v. *Morton Int'l, Inc.*, 113 S. Ct. 1967, 1971 (1993).

The Federal Circuit has from time to time rendered decisions that have been criticized, even by judges of the Court itself, as usurping the fact-finding role of the Dis-

trict Courts. *See, e.g., Malta* v. *Schulmerich Carillons, Inc.*, 952 F.2d 1320, 1331 (Fed. Cir. 1991) (Newman, J., dissenting) (criticizing the majority for rejecting a jury verdict and making a *de novo* determination of the factual issue of infringement), *cert. denied*, 112 S. Ct. 2942 (1992).

This Court has previously considered—and limited—the role of the Federal Circuit in reviewing questions of fact underlying the issue of patent validity. *Dennison Mfg. Co.* v. *Panduit Corp.*, 475 U.S. 809 (1986). Although patent validity ultimately is a question of law, it necessarily involves several basic factual questions. *Graham* v. *John Deere Co.*, 383 U.S. 1, 17 (1966).

In *Dennison*, the Federal Circuit reversed a District Court finding of patent invalidity without referring to Rule 52(a) of the Federal Rules of Civil Procedure or explaining why the District Court was "clearly erroneous" under the Rule 52(a) standard of review of factual questions. Bereft of an opinion of the Federal Circuit on the complex relationship between the factual issues and the ultimate determination of validity, this Court summarily vacated the judgment of the Court of Appeals and remanded the case for further consideration in light of Rule 52(a).

The present case concerns the role of the Federal Circuit in reviewing questions of fact underlying the issue of patent *infringement* and raises a similar issue. It is imperative that the Federal Circuit review patent infringement decisions, as well as decisions on validity, in a manner consistent with Rule 52(a). As set forth below, however, the panel majority in this case made two related errors, each of which intruded upon the assigned role of the District Court to find the facts.

Like the issue raised in *Dennison*, the issue of judicial administration raised in this petition is of significant importance to the Federal Circuit's review of decisions in patent cases nationwide. Review by this Court is there-

fore warranted, not on the substantive patent issues which the Court need not address, but on the proper allocation of functions between the Federal Circuit and the District Courts.

I. THE FEDERAL CIRCUIT ERRED IN RELYING UPON THE HARMLESS ERROR DOCTRINE TO AFFIRM A FINDING OF NONINFRINGEMENT AFTER REJECTING THE "BASIC REASON" FOR THE DISTRICT COURT'S DECISION

Under the harmless error doctrine of 28 U.S.C. § 2111, a Court of Appeals need not reverse a decision of a District Court based on errors that "do not affect the substantial rights of the parties." This Court has articulated the following standard to be used in determining whether an error is harmless:

> [I]f one cannot say, with fair assurance, after pondering all that happened without stripping the erroneous action from the whole, that the judgment was not substantially swayed by the error, it is impossible to conclude that substantial rights were not affected. The inquiry cannot be merely whether there was enough to support the result, apart from the phase affected by the error. It is rather, even so, *whether the error itself had substantial influence*.

Kotteakos v. *United States*, 328 U.S. 750, 765 (1946) (interpreting old 28 U.S.C. § 391) (emphasis supplied).

Here, it is clear from the District Court's opinion itself that the error was not harmless. The District Court stated that "the case is a close one," App. at 29a; 24 U.S.P.Q.2d at 1898, and identified the article and speech as "*the basic reason* why I am holding in favor of the defendants on the question of interpretation." App. at 39a; 24 U.S.P.Q.2d at 1902 (emphasis supplied). It cited the nature of Jennings' research, as described in the article and speech, as "[p]erhaps *the most important point* in the evidence." App. at 35a; 24 U.S.P.Q.2d at 1901 (emphasis supplied).

When the majority of the Federal Circuit panel held that reliance on this evidence was impermissible, however, it did not address whether the District Court's reliance on this evidence had a "substantial influence" on its decision within the meaning of *Kotteakos* and 28 U.S.C. § 2111. Had it done so, it would have had to agree with the dissenting judge that "[w]ithout *the primary source of evidence upon which the district court based its decision*, this 'very close' case would no doubt have ended differently." App. at 18a; 7 F.3d at 1580 (Rader, J., dissenting) (emphasis supplied).

II. THE PANEL MAJORITY ALSO ERRED BY DECIDING FACTUAL QUESTIONS IN INTERPRETING THE CLAIMS OF THE PATENT

The majority of the Federal Circuit panel held that the District Court's reliance on Jennings' article and speech was harmless error by improperly determining questions of fact confided to the District Court. Determination of patent infringement requires interpretation of the scope and meaning of a patent's claims and application of the properly construed claims to the allegedly infringing product. The first of these questions is ultimately a question of law, and the second is a question of fact. *E.g., Winas* v. *Denmead*, 56 U.S. (15 How.) 330, 338 (1853).

Even though patent claim interpretation is a question of law, as here it often involves underlying questions of fact, like the question of patent validity addressed in *Dennison*. Over 100 years ago, this Court held:

> Where the specification and claim, both in the original and reissued patents, are expressed in ordinary language, without employing any technical terms or terms of art, the question whether the reissued patent is for the same invention as that described in the original patent or for a different one is purely a question of construction, but where both or either contain *technical terms or terms of art* the court may hear

> the testimony of scientific witnesses to aid the court in coming to a correct conclusion. Cases doubtless arise where the language of the specification and claim, both of the surrendered and reissued patents, is so interspersed with technical terms and terms of art that *the testimony of scientific witnesses is indispensable to a correct understanding of its meaning.* Both parties in such a case would have a right to examine such witnesses, and it would undoubtedly be error in the court to reject the testimony . . . .

Seymour v. *Osborne*, 78 U.S. (11 Wall.) 516, 546 (1870) (emphasis supplied).

More recently, the Federal Circuit has recognized exactly this point:

> Claim interpretation is a question of law, *having factual underpinnings.* When the meaning of key terms of claims is disputed, as in this case, extrinsic evidence may be adduced including testimony of witnesses, and reference may be had to the specification, the prosecution history, prior art, and other claims.

Tandon Corp. v. *U.S. Int'l Trade Comm'n*, 831 F.2d 1017, 1021 (Fed. Cir. 1987) (affirming I.T.C. finding of noninfringement) (emphasis supplied).

Thus, the Federal Circuit has acknowledged the limitations on its role in reviewing matters of patent claim interpretation:

> Claim construction is reviewed as a matter of law. However, *interpretation of a claim may depend on evidentiary material about which there is a factual dispute, requiring resolution of factual issues as a basis for interpretation of the claim.* In this case, there was extensive testimony on the issue of claim construction, including the conflicting views of experts on both legal and factual questions. *Those factual considerations that are pertinent to the district court's construction of the term "bottomless" are reviewed under the clearly erroneous standard.*

H.H. Robertson, Co. v. *United Steel Deck, Inc.*, 820 F.2d 384, 389 (Fed. Cir. 1987) (affirming District Court finding of infringement) (citations omitted) (emphasis supplied).

But, as shown by the present case, that acknowledgment "keep[s] the word of promise to our ear [a]nd break[s] it to our hope," [1] unless the Federal Circuit is required to observe proper standards of review.

As held in this Court's *Dennison* decision, it is error for the Federal Circuit to decide questions of law involving underlying disputed facts without regard to the factual findings of the District Court and the "clearly erroneous" standard for reviewing those fact findings under Rule 52(a) of the Federal Rules of Civil Procedure. *Dennison*, 475 U.S. at 811.

The proper construction of the patent claims at issue involves the interplay between the phrase "linked . . . to a terminal portion of the polysaccharide" and the recitation in the claims of a specific species of bacterium (*Haemophilus influenza*) as understood by one skilled in the art in light of the patent specification.

The panel majority, instead of remanding to the District Court to make findings based upon the evidence properly before it, independently determined factual questions without the benefit of having sat through three weeks of trial and hearing the testimony of ~~six~~ five scientific witnesses on the dispositive issues. This scientific testimony was "indispensable" to a correct understanding of the meaning of the claims under the teaching of *Seymour* v. *Osborne*, and it was for the District Court, not the reviewing court, to make the proper findings. But, after making findings as to what the specification did or did not teach, an inherently fact-based issue, the panel majority chose to credit the testimony of one of the respondents' expert wit-

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[1] William Shakespeare, *Macbeth*, act 5, sc. 7.

nesses, whom they never saw, and whose testimony contradicts a finding of the District Court. App. at 10a-11a; 7 F.3d at 1577. The District Court specifically stated that *it* would not rely upon the testimony of this witness in interpreting the patent and instructed counsel for the petitioner that he need not cross examine the witness regarding interpretation. Trial transcript of Aug. 20, 1992 at 1447.

In deciding how to reconcile the terms of the patent claims independently of the District Court, based on a selective reading of the evidence adduced at trial, the panel majority improperly decided the disputed facts underlying the interpretation of the patent claims.

III. THE FEDERAL CIRCUIT'S ERRORS EACH UNDERMINED THE FACT FINDING ROLE OF THE DISTRICT COURT

In this case, the majority's misapplication of the harmless error doctrine of 28 U.S.C. § 2111 undermined the role of the District Court to determine disputed facts by denying the District Court the opportunity to weigh only the evidence properly before it in reaching a decision. As the dissent recognized, given the closeness of the case, it is likely that the District Court would have reached a different decision if it had had this opportunity. The Federal Circuit made an even more direct assault on the fact-finding role of the District Courts, as set forth in Rule 52(a), by evaluating witness credibility and deciding factual questions for itself.

Preserving the proper fact finding role of the District Courts serves important public purposes:

> The rationale for deference to the original finder of fact is not limited to the superiority of the trial judge's position to make determinations of credibility. The trial judge's major role is the determination of fact, and with experience in fulfilling that role comes expertise. Duplication of the trial judge's efforts in the

> court of appeals would very likely contribute only negligibly to the accuracy of fact determination at a huge cost in diversion of judicial resources.

Anderson v. *City of Bessemer City*, 470 U.S. 564, 574-75 (1985).

Especially given the unique nationwide appellate jurisdiction of the U.S. Court of Appeals for the Federal Circuit, it is important that this Court provide guidance and direction to prevent future usurpation of the District Courts' fact finding role in patent infringement cases. The present case affords the vehicle for doing so in a specialized but highly important area of the law, in which bench, bar and litigants all have a strong interest in knowing the procedural rules by which they must live.

CONCLUSION

For the foregoing reasons, petitioners respectfully request that this petition for a writ of certiorari be granted.

Respectfully submitted,

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APPENDIX

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UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

93-1076

NORTH AMERICAN VACCINE, INC. and
NATIONAL RESEARCH COUNCIL OF CANADA,
Plaintiffs-Appellants,

v.

AMERICAN CYANAMID COMPANY and
PRAXIS BIOLOGICS, INC.,
Defendants-Appellees.

Appealed from U.S. District Court
Southern District of New York

DECIDED: October 6, 1993

Before LOURIE, *Circuit Judge*, SKELTON, *Senior Circuit Judge*, and RADER, *Circuit Judge*.

LOURIE, *Circuit Judge*.

National Research Council of Canada and its exclusive licensee, North American Vaccine (collectively NRC), appeal from the judgment of the United States District Court for the Southern District of New York holding claims 12 and 25 of U.S. Patent 4,356,170 invalid for

indefiniteness under 35 U.S.C. § 112, ¶ 2 (1988), and not infringed by American Cyanamid Co. and Praxis Biologics, Inc. (collectively Cyanamid). *North American Vaccine, Inc. v. American Cyanamid Co.*, 24 USPQ2d 1898 (S.D.N.Y. 1992). We affirm-in-part and reverse-in-part.

BACKGROUND

On February 28, 1991, NRC brought an action against Cyanamid alleging infringement of the '170 patent. That patent, entitled "Immunogenic Polysaccharide-Protein Conjugates," relates to human infant vaccines against bacterial infections such as meningitis. The principal components of the vaccines are polysaccharide-protein conjugates. The polysaccharide, which is derived from the bacteria against which immunization is sought, has antigenic properties that elicit an immune response. Infant immune systems, however, do not respond well to the polysaccharide unless it is linked to a protein.

While linking of the polysaccharide and protein enhances infants' immune response to the antigenic polysaccharide, the immune response is hampered by "crosslinking." The parties indicate that crosslinking obstructs the antigenic sites of the polysaccharide, precluding an effective immune response. The amount of crosslinking increases with the number of proteins that are linked to the polysaccharide. The claimed invention purports to avoid the problem associated with crosslinking by linking the protein only to a terminal portion of the polysaccharide, thereby preserving the antigenic properties of the polysaccharide and producing an immune response in infants. The meaning of the expression "a terminal portion" in the claims is a key issue in this case. The meaning of the term "crosslinking" is also contested.

Trial was limited to the issues of infringement and validity of claims 12 and 25, which are directed, respectively, to a polysaccharide-protein conjugate and a human

infant vaccine comprising that conjugate. Both are dependent upon claim 11, which reads:

> 11. An antigenic-polysaccharide-protein conjugate wherein the polysaccharide and protein are covalently linked through a
>
> CH_2-NH-protein
>
> *linkage to a terminal portion of the polysaccharide without significant crosslinking*, said antigenic polysaccharide having a MW [molecular weight] above about 2,000.

(emphasis added). Claims 12 and 25 read as follows:

> 12. The conjugate of claim 11 wherein the antigenic polysaccharide is selected from the group derived from meningococci, *Haemophilus influenza*, pneumococci, beta-hemolytic streptococci, and E. coli.
>
> 25. A human infant vaccine comprising the conjugate of claim 11 wherein the polysaccharide comprises at least one of meningococcal polysaccharide and *Haemophilus influenza polysaccharide*.

(emphasis added).

A polysaccharide is a sugar molecule having a carbon backbone with hydroxy groups attached, to which proteins may be linked. Linking a protein to a polysaccharide generally involves modifying the hydroxy groups to create one or more active sites and covalently linking the activated polysaccharide to a free amino group of a protein. The result is a polysaccharide-protein conjugate.

Cyanamid's accused product, "HibTITER," is a vaccine against *Haemophilus influenza* (*H. flu*) type b (Hib) bacteria that can cause meningitis. HibTITER consists of Hib polysaccharides linked to one or more proteins. Specifically, it is comprised of three components referred to as "monomers," "dimers," and "trimers." Monomers,

which constitute 50% of the polysaccharide-protein molecules of HibTITER, consist of a single protein linked to a terminal end of one or more polysaccharides; dimers consist of two proteins linked together by polysaccharide; and trimers consist of three proteins linked together by polysaccharides. The protein linkage in each of these components is at a terminal portion of the Hib polysaccharide; none has a protein linkage along the backbone of the polysaccharide. Monomers, having a protein linkage at only one terminal, are referred to as monofunctional. Dimers and trimers, having linkages at both terminals of the polysaccharide, are referred to as difunctional and exhibit what has been called end-to-end cross-linking.

The district court entered judgment for Cyanamid, holding that claims 12 and 25 were not infringed and were invalid for indefiniteness under 35 U.S.C. § 112, second paragraph. NRC appeals from that judgment.

DISCUSSION

A. *Infringement*

A determination of patent infringement requires a two-step analysis. First, a claim must be interpreted to determine its proper scope and meaning; second, it must be determined whether an accused device is within the scope of the properly interpreted claim. *ZMI Corp. v. Cardiac Resuscitator Corp.*, 844 F.2d 1576, 1578, 6 USPQ2d 1557, 1559 (Fed. Cir. 1988). The first step is an issue of law and the second a question of fact. *Minnesota Mining & Mfg., Co. v. Johnson & Johnson Orthopaedics, Inc.*, 976 F.2d 1559, 1570, 24 USPQ2d 1321, 1330 (Fed. Cir. 1992) (citations omitted). A determination of literal infringement requires that each limitation in the asserted claims be present in the accused device. *Hi-Life Products., Inc. v. American Nat'l Water-Mattress Corp.*, 842 F.2d 323, 325, 6 USPQ2d 1132, 1133 (Fed. Cir. 1988). Only the issue of literal infringement is before us in this case.

Whether HibTITER, which includes monomers, dimers, and trimers, infringes claims 12 and 25, turns on our interpretation of the limitation "linkage to a terminal portion of the polysaccharide without significant crosslinking" in claim 11. It is not disputed that the monomer components in HibTITER meet this limitation. Thus, if, contrary to what the district court decided,[1] the monomers themselves meet all the other limitations of the claims, including being a conjugate, infringement of the claims would be established because they contain "linkage to a terminal portion of the polysaccharide without significant crosslinking" and they are quantitatively a significant component of the product. However, at oral argument, counsel for NRC stated that NRC is not contesting this aspect of the court's decision.[2] The only issue

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[1] The court rejected NRC's argument that infringement is established on the basis of the monomers alone. NRC had asserted that "conjugate" in claim 11 referred to an individual molecule and that HibTITER infringed since each monomer molecule was within the scope of the asserted claims.

[2] At oral argument, Judge Lourie asked counsel for NRC about the meaning of the word "conjugate" in the claims. Counsel for NRC responded:

> Well, the word "conjugate" was in dispute at trial, and my brother Mr. Dunner has made an issue of it on appeal, but it is really not an issue *because we are not contesting the district court's interpretation of the word conjugate.* The district court interpreted the word "conjugate" as embracing all the molecules in the mixture and therefore and [sic] the accused product really has three types of molecules. It has so-called monomers, which have no cross-linking, and it has dimers and trimers which have the end-to-end cross-linking. And we have an argument below that the monomers should infringe irrespective of the dimers and trimers. And the district court rejected that because he said, "no, the word conjugate embraces the entire mixture." But, we are not contesting that on our primary argument on appeal. Our primary argument on appeal is that not only the monomers with no cross-linking, but the dimers and the trimers, which have only end-to-end cross-linking, meet all the limitations of the claims. They have a linkage to a terminal portion without significant cross-

before us, therefore, is whether the other components of the vaccine, the dimers and trimers which have protein linkages at both terminal portions of the Hib polysaccharides and exhibit end-to-end crosslinking, come within the meaning of the above-quoted language, in which case the totality of the accused product would be infringing.

The district court construed this phrase as being limited to linkage at only one terminal portion of the polysaccharide, excluding all crosslinking, even end-to-end crosslinking. Accordingly, the court held that the claims did not cover the dimers and trimers in HibTITER. NRC argues that the court's claim interpretation was erroneous and that the limitation requiring "linkage to a terminal portion of the polysaccharide without significant crosslinking" in claim 11 is not limited to linkage at only a single terminal, but includes linkages at either one or both terminals of the polysaccharide. According to NRC, end-to-end crosslinking which involves linkages at both terminal portions of the polysaccharide is not "significant crosslinking" for purposes of the asserted claims since it achieves the intended purpose of the invention by avoiding crosslinking along the backbone of the polysaccharide. NRC also argues that the inclusion of references to *Haemophilus influenza* in dependent claim 12 and the specification indicate that claim 11 was intended to be interpreted to include end-to-end crosslinking because polysaccharides from that organism lead to end-to-end crosslinking. Thus, NRC asserts, the properly interpreted claims cover the dimers and trimers in HibTITER. We disagree and conclude that the contested phrase does not include polysaccharide-protein linkages at both terminal portions of the polysaccharide.

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linking. And therefore, when the claims are properly construed, then all the molecules in the entire product meet the limitations of the claim, irrespective of whether conjugate means a single molecule or all the molecules. *So I don't think conjugate is really an issue on this appeal, your Honor.*

Transcript from oral argument (emphases added).

A determination as to the scope and meaning of a claim is a question of law which we review *de novo*. *ZMI*, 844 F.2d at 1578, 6 USPQ2d at 1559. Therefore, we need not defer to the district court's claim interpretation. *Specialty Composites v. Cabot Corp.*, 845 F.2d 981, 986, 6 USPQ2d 1601, 1604 (Fed. Cir. 1988) (citation omitted). Cyanamid characterizes these issues as questions of fact, imposing on us a "clearly erroneous" standard of review. It argues that the meaning of claim language raises factual questions. We agree that a genuine evidentiary conflict underlying the meaning of claim terms raises a question of fact, but the questions before us in this case go to the heart of what the claims mean. Resolution of disputed issues regarding the meaning of contested language is ultimately a determination of what claims mean and what they cover. It is a matter of law for this court to decide without special deference to the district court. Absent "a genuine evidentiary conflict created by the underlying probative evidence pertinent to the claim's interpretation[,] . . . claim interpretation may be resolved as an issue of law by the court taking into account the specification, prosecution history or other evidence . . . ." *Johnston v. IVAC Corp.*, 885 F.2d 1574, 1579-80, 12 USPQ2d 1382, 1386 (Fed. Cir. 1989) (citations omitted).

In construing claims, we begin with the language of the claims themselves. *SmithKline Diagnostics, Inc. v. Helena Lab., Corp.*, 859 F.2d 878, 882, 8 USPQ2d 1468, 1472 (Fed. Cir. 1988) (citations omitted). Claim 11 specifically refers to "a terminal portion"; it does not refer to "any terminal portion" or to "all terminal portions." While it is generally accepted in patent parlance that "a" can mean one or more, *see* Robert C. Faber, *Landis on Mechanics of Patent Claim Drafting* 531 (3d ed. 1990) ("In a claim, the indefinite article A or AN connotes 'one or more.' "), there is no indication in the patent specification that the inventors here intended it to have other than its normal singular meaning.

When the meaning of a claim term is in doubt, we look to the specification for guidance. *See Hormone Research Foundation, Inc. v. Genentech, Inc.*, 904 F.2d 1558, 1562, 15 USPQ2d 1039, 1042 (Fed. Cir. 1990), *cert. dismissed*, 111 S. Ct. 1434 (1991). In doing so here, we find no indication in the patent specification that the inventors intended to included end-to-end linkages within the scope of their invention. All references to polysaccharide linkages speak of a linkage, not multiple linkages. For example, the summary of the invention describes the formation of the protein linkage to a terminal portion of the polysaccharide as follows:

> We have found it possible to introduce *a free aldehyde group* into the polysaccharide molecule in *a terminal location* and to specifically couple *this aldehyde group* to protein without activating other functional groups on the polysaccharide.

Col. 2, lines 33-37 (emphasis added.) Similarly, the specification states:

> The reductive amination covalently couples *the terminal aldehyde group* of the polysaccharide to a free amino group on the protein through *a* $-CH_2NH-$ *protein linkage where the* $-CH_2-$ *derives from the aldehyde group*. There is no significant cross-linking by this method . . . .

Col. 3, lines 55-64 (emphasis added.) Reference to "the" terminal aldehyde group is consistent with linkage at only one terminal, not at both.

The examples in the specification also support linkage at only one terminal. In teaching the selective periodate oxidation of meningococcal polysaccharide, the specification states that "[t]he oxidized polysaccharides now had a terminally-located aldehyde group." Col. 5, lines 14-15. Use of the term "a" and reference to "group" in the singular shows that the specification teaches linkage at only one terminal portion. Furthermore, in teaching the

direct conjugation of the oxidized polysaccharides with proteins, the specification states:

> *It is unlikely that the reducing terminal sialic acid residue at the opposite end would oxidize to any great extent* using these conditions because it exists in solution mainly in its pyranose ring form and such has been found to behave similarly to an interchain residue.

Col. 5, lines 50-54 (emphasis added.) This statement shows that it is "unlikely" to obtain linkage at both terminals. Similarly, with respect to meningococcal group A polysaccharide, the specification teaches:

> *[T]he reducing end-group N-acetyl-mannosamine residue was made into the most susceptible residue* by simply reducing it to its open chain N-acetylmannosaminitol derivative. In this form, the modified group A polysaccharide was selectively oxidized *at this residue* to generate *a terminally-located aldehyde group.*

Col. 5, line 67—col. 6, line 5 (emphases added.) Again, reference to "the" reducing end group, "this" residue, and "a" terminal aldehyde are consistent with linkage in the singular.

NRC argues that the "significant crosslinking" that the inventors intended to avoid was not end-to-end crosslinking, but crosslinking across the backbone of the polysaccharide molecule. While such an interpretation might make sense as a theoretical concept, it has no support in the specification. The word "backbone" does not appear in the specification, nor does the concept of avoiding linking other than at multiple terminal portions. Contrary to NRC's argument that "significant crosslinking" is crosslinking along the backbone of the polysaccharide, the specification states:

> The reductive amination covalently couples *the terminal aldehyde group* of the polysaccharide to a free

> amino group on the protein . . . . *There is no significant cross-linking by this method* . . . .

Col. 3, lines 55-64 (emphases added.) The above-referenced statement that linkage to *the* terminal portion results in "no significant crosslinking" shows that "significant crosslinking" for purposes of the claims was not intended to mean linking along the backbone as NRC urges, but linking at more than one terminal.

It is the responsibility of patent applicants to disclose their inventions adequately. 35 U.S.C. § 112. There is no such disclosure of the concept of avoiding crosslinking along the backbone in this patent. Thus, an invention of that breadth does not meet the *description requirement. See Carmen Industries, Inc. v. Wahl*, 724 F.2d 932, 937 n.5, 220 USPQ 481, 485 n.5 (Fed. Cir. 1983) ("Claims should be so construed, if possible, as to sustain their validity.") (citations omitted). As explained above, the examples are consistent with monofunctionality, not difunctionality. A patent applicant cannot disclose and claim an invention narrowly and then, in the course of an infringement suit, argue effectively that the claims should be construed to cover that which is neither described nor enabled in the patent. One of the inventors, Dr. Jennings, testified that he intended to include difunctional molecules within the scope of his invention. Such after-the-fact testimony is of little weight compared to the clear import of the patent disclosure itself. *See Senmed, Inc. v. Richard-Allen Medical Indus. Inc.*, 888 F.2d 815, 819 n.8, 12 USPQ2d 1508, 1512 n.8 (Fed. Cir. 1989) (Where meaning of claim term is clear from specification and prosecution history, the inventor's "self-serving *post-hoc* opinion testimony on the legal question [] whether it should have a different meaning was of little if any significance.") (citation omitted).

NRC argues that inclusion of the words *Haemophilus influenza* in the dependent claims and specification prove

that difunctional molecules are within the scope of claim 11 because such organisms lead to difunctional products according to this invention. While it is true that dependent claims can aid in interpreting the scope of claims from which they depend, they are only an aid to interpretation and are not conclusive. The dependent claim tail cannot wag the independent claim dog. Certainly in this case, as we have indicated, there is no further disclosure or description in the specification of difunctional molecules resulting from *H. flu* or any other organism. Moreover, the district court did not find that *H. flu* always yields a difunctional result, as NRC asserts, but found that one of the "five or six" *H. flu* serotypes "is the one which yields the difunctional result." 24 USPQ2d at 1903.

There also was evidence at trial contrary to NRC's assertion that use of *H. flu* always results in difunctionality. Dr. Eby, one of Cyanamid's expert witnesses, testified that the *H. flu* polysaccharide could be treated to create only a single aldehyde that would result in monofunctionality and that such monofunctional *H. flu* polysaccharides could have been made by one skilled in the art in 1981 when the patent application was filed. Dr. Eby explained that the reference to *H. flu* in claim 12 is completely consistent with monofunctionality, thereby providing a basis for its inclusion consistent with the otherwise clear singular meaning of "a terminal portion." Thus, use of the words *Haemophilus Influenza* in claims 12 and 25 is not inconsistent with a monofunctional interpretation of claim 11.

Finally, if we were to interpret claim 11 on the basis of NRC's argument concerning what claim 12 requires, claim 11 would include polyfunctional molecules, which are concededly not within the scope of the invention. That cannot be what NRC intends. We therefore conclude that "linkage to a terminal portion" includes linkage only to "a terminal portion" at one end of the polysaccharide.

Since we have interpreted the expression "a terminal portion" to include only monofunctionality, it is clear that the limitation "without significant crosslinking" excludes from the claims linkage other than monofunctional linkage. End-to-end crosslinking, consisting of protetin linkages at both terminal portions of a polysaccharide, is inconsistent with the clear meaning of the expression "a terminal portion." Thus, end-to-end crosslinking is "significant crosslinking" in terms of this patent and it is excluded from the claims. As noted earlier, the specification does not use the term end-to-end crosslinking or difunctionality, nor does it use any language which conveys that backbone crosslinking was excluded, but end-to-end crosslinking was not. As for the term "significant," it is undisputed that 50% of the polysaccharide-protein molecules are other than monofunctional, that they have end-to-end crosslinking. There is no basis for concluding that 50% is not significant. Finally, it is the responsibility of patent applicants to define their inventions adequately. In the absence of any definition of this term in the specification, NRC cannot complain if its after-the-fact definition is not accepted. Thus, the district court correctly construed the claim in concluding that end-to-end crosslinking did not meet the limitations of the claims.

Cyanamid, as did the district court, emphasizes an article and speech of Dr. Jennings, one of the named inventors on the patent, in which he described his research on polysaccharide-protein conjugates as directed toward achieving monofunctionality. Jennings made these presentations at about the same time as he filed his patent application. The court concluded that Jennings' failure to clearly express in his application his intention to claim more than the monofunctional product of his earlier work showed that the claims were limited to the scope of his earlier work. 24 USPQ2d at 1902.

Cyanamid argued before us that the court correctly concluded that the monofunctional approach embodied in

Jennings earlier work was carried over into his patent. According to Cyanamid, Jennings' article and speech show the "evolution" of the patent and compel a claim construction to require monofunctionality. While we have affirmed the district court's interpretation of the claims, we must reject its doing so on the basis of this argument. A patent is to be interpreted by what it states rather than by what the inventor wrote in a scientific publication.

There is no inconsistency between writing a paper (or giving a speech) on a particular embodiment of an invention and then claiming one's invention more broadly in a patent application. Patents often teach embodiments not carried out in the laboratory; scientific papers rarely do. Thus, it was error, albeit harmless error, for the distict court to conclude that the narrow scope of the article limits the scope of the patent claims, which should be judged on their own merits.

Having construed the claims, the next determination is infringement. Accordingly, we must determine whether the court clearly erred in holding that the claims do not read on HibTITER. As stated above, the characteristics of HibTITER are undisputed. The only issue is whether the phrase "linkage to a terminal portion of the polysaccharide without significant crosslinking" reads on the HibTITER product as a whole, which, in view of NRC's concession at oral argument,[3] requires determination whether the phrase reads on a product which includes dimers and trimers as well as monomers. In view of our decision that this phrase covers linkage at only one terminal portion of the polysaccharide and does not include

[3] The dissent, in its commentary on claim 25, ignores the clear and unmistakable concession by NRC that it is not challenging the trial court's ruling that "conjugate" means the mixture of molecules as opposed to individual molecules. Whatever NRC's reasons, we do not review what it chooses to accept. Moreover, if claim 11 is not infringed, as we have concluded, dependent claim 25 cannot be.

end-to-end crosslinking, the HibTITER product including dimers and trimers clearly is not within the scope of the claims. Accordingly, the district court did not clearly err in concluding that HibTITER does not infringe claims 12 and 25.[4]

B. *Validity*

The district court concluded that claims 12 and 25 were invalid for indefiniteness under 35 U.S.C. § 112, second paragraph, which requires that the "specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention." Even though we have affirmed the district court's decision of noninfringement, we find it desirable to review this holding of invalidity. *See Cardinal Chem. Co. v. Morton Int'l, Inc.*, 113 S. Ct. 1967, 26 USPQ2d 1721 (1993). NRC is entitled to have the validity of its claims considered rather than have the district court's judgment merely vacated, leaving a cloud on the patent. Future modification of Cyanamid's product, or sale by another party, could raise questions of infringement of the claims as we and the district court have construed them. Finally, since we have thoroughly reviewed the case, no added judicial effort is involved.

The underlying basis for the court's conclusion of invalidity on the ground of indefiniteness was the parties' stipulation that the five categories of polysaccharides recited in claim 12, and the two categories recited in claim 25, each include a number of members (serotypes) which, when treated according to the teachings of the '170 patent, would result in polyfunctional molecules, polysaccharides

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[4] The dissent argues at great length that the specification "reveals the inventors' intent" that cross-linking only means backbone cross-linking, and that "a terminal portion" includes two terminal portions. It refers to the specification's "clear meaning" and that it "clearly did not limit the claims." The plain fact, however, is that these matters are not clear at all and that the specification contains no express disclosure of difunctional molecules.

having protein linkage along their backbones. This result is outside the scope of claim 11 and contrary to the teachings of the patent. On the basis of this fact, the court held the claims indefinite, stating that "there are so many different kinds of polysaccharides referred to which would yield different results, polyfunctional, difunctional and monofunctional, some of which results are admittedly contrary to the patent's teaching." 24 USPQ2d at 1903. NRC argues that the court's conclusion was erroneous. Specifically, NRC asserts that Cyanamid failed to meet its burden of proving that the claims are indefinite, and that the parties' stipulation was an insufficient basis for the court's holding that the claims are invalid. We agree with NRC that the parties' stipulation of possible inoperativeness of some species does not constitute an admission that those skilled in the art would not be reasonably apprised of the scope of the claims.

Under 35 U.S.C. § 282 (1988), a patent is presumed valid, and at trial Cyanamid had the burden of proving facts by clear and convincing evidence showing that the patent is invalid. *See Buildex, Inc. v. Kason Indus., Inc.*, 849 F.2d 1461, 1463, 7 USPQ2d 1325, 1326-27 (Fed. Cir. 1988). Compliance with the definiteness requirement is a question of law which we review *de novo*. *Carl Zeiss Stiftung v. Renishaw plc*, 945 F.2d 1173, 1181, 20 USPQ2d 1094, 1101 (Fed. Cir. 1991). Whether a claim is invalid for indefiniteness depends on whether those skilled in the art would understand the scope of the claim when the claim is read in light of the specification. *Orthokinetics, Inc. v. Safety Travel Chairs, Inc.*, 806 F.2d 1565, 1576, 1 USPQ2d 1081, 1088, (Fed. Cir. 1986) (citations omitted).

Cyanamid did not meet its burden under the clear and convincing standards to show that one of ordinary skill would not understand what is included within claims 12 and 25. Claim 11, the claim from which claims 12 and 25 depend, requires linkage at a terminal portion of the

polysaccharide. The specification is clear that the claimed invention relates to conjugates having a protein linkage at a single terminal portion of the polysaccharide, not at both terminal portions. Thus, while the parties in the midst of a dispute have disagreed concerning the meaning of the claims, the claims are not so lacking in clarity as to be invalid under section 112.

The categories of polysaccharides recited in claims 12 and 25 do include numerous members (serotypes), some of which apparently result in polyfunctional molecules when treated according to the teachings of the patent. The fact that dependent claims include species which might not meet the objects of the invention does not by itself prove that one skilled in the art cannot ascertain the scope of the asserted claims. That objection goes to possible inoperativeness under 35 U.S.C. § 101 or lack of enablement under 35 U.S.C. § 112, first paragraph, neither of which provisions are before us. Moreover, if a species within a dependent claim does not meet the limitations of the independent claim, arguably it is not included within the scope of that dependent claim.

The law is clear that " '[i]f the claims, read in the light of the specification[s], reasonably apprise those skilled in the art both of the utilization and scope of the invention, and if the language is as precise as the subject matter permits, the courts can demand no more." *Shatterproof Glass Corp. v. Libbey-Owens Ford, Co.*, 758 F.2d 613, 624, 225 USPQ 634, 641 (Fed. Cir.), *cert. dismissed*, 474 U.S. 976 (1985) (quoting *Georgia-Pacific Corp. v. United States Plywood Corp.*, 258 F.2d 124, 136, 118 USPQ 122, 132 (2d Cir.), *cert. denied*, 358 U.S. 884 (1958)). That is the case here.

NRC's expert, Dr. Schoolnik, testified on cross-examination that, in view of the teaching in the specification to avoid protein linkage along the backbone of the polysaccharide, he would know that the polysaccharides recited in claims 12 and 25 refer only to the serotypes

that would result in "a clean backbone when the procedures recommended by [the] patent are performed on those structures." He testified:

> [I]t's understood by everyone working in the field that you first draw out from [the group of bacterial types in claim 12] the particular types that are relevant to infantile meningitis, and then I think, as a scientist, I would look at the structure of the polysaccharides from those types and I would say are they structures that would, when subjected to this process, leave a backbone that's antigenic and probably, therefore, effective as a vaccine.

We conclude that the claims are sufficiently clear to apprise those skilled in the art of their scope. We thus reject Cyanamid's argument that indefiniteness "follow[s] directly from stipulated facts," as that stipulation was insufficient as a matter of law to sustain the court's holding that claims 12 and 25 are indefinite. Accordingly, we conclude that the court erred in its holding of invalidity.

CONCLUSION

The court did not err in holding claims 12 and 25 of the '170 patent not infringed, but did err in holding them invalid. Accordingly, the judgment of the district court is affirmed-in-part and reversed-in-part.

COSTS

No costs.

AFFIRMED-IN-PART AND REVERSED-IN-PART

RADER, *Circuit Judge*, dissenting.

I agree with this panel that the district court erroneously concluded that claims 12 and 25 were invalid for indefiniteness. I also agree that the district court erred in relying on the inventors' scientific articles to determine the scope of the claims. Unfortunately, I cannot support the rest of this court's opinion.

As the panel points out, the district court erroneously based its decision on the inventors' articles in scientific journals. Although a patent specification may supply guidance about the meaning of claim terms, *Hormone Research Foundation v. Genentech, Inc.*, 904 F.2d 1558, 1562, 15 USPQ2d 1039, 1043 (Fed. Cir. 1990), scientific literature differs in purpose, scope, and legal effect from patent writings. Because inventors generally have extraordinary skill, their scientific writings outside the patent are rarely even a source of knowledge about ordinary skill in the art. The panel's opinion correctly notes the trial court's error in relying extensively on the inventors' scientific articles for its claim interpretation. The trial court referred to the scientific writings as "the most important point in the evidence." Surprisingly, however, the panel's opinion did not consider this error a cause for reversal. In a case the district court repeatedly characterized as "very close," this extensive reliance on impermissible evidence constitutes reversible error. Without the primary source of evidence upon which the district court based its decision, this "very close" case would no doubt have ended differently.

The majority suggests that the meaning of the term "conjugate" was conceded by North American Vaccine. In context, however, it appears that counsel was only trying to argue that the interpretation of the term "conjugate" is not dispositive. Moreover, plaintiff's reply brief actually contests the majority's interpretation and argues that the district court's ruling was incorrect. The majority hinges its conclusion on an equivocal statement

made to pursue a more important concern. This approach appears unwarranted under the circumstances.

Claim 11—"at a terminal portion"

An examination of the claim language shows that the district court's use of impermissible evidence infected the judgment in this case. Claim 11 requires linkage of a protein "to a terminal portion of the polysaccharide." The accused product literally reads on this requirement. The panel's opinion and both parties concede: "The protein linkage in each of these components is at *a terminal portion* of the Hib polysaccharide . . . ." Slip Op. at 4, lines 8-10.

A branched polysaccharide, however, can have two or more terminal ends. The accused product linked protein at two of these terminal ends. The trial court, relying on the inventors' scientific writings about "monofunctionality" or "monovalency" (technical terms for linkage at a single terminal end), interpreted the claim language to mean that any more than a single link at a terminal end escapes infringement.

The claim, however, does not require linkage "at a *single* terminal portion of the polysaccharide," but simply "at a terminal portion." The trial court used extraneous scientific writings to create a limitation—at a *single* terminal portion—not found in the claim language. Indeed in patent claims, the indefinite article "a" may denote one or more objects. Robert C. Faber, *Landis on Mechanics of Patent Claim Drafting* 531 (3d ed. 1990) ("In a claim, the indefinite article A or AN connotes 'one or more' ").

Thus, according to the claim language, each link at a terminal portion of the polysaccharide reads on the claims. American Cyanamid infringed the patent by linking a protein to "a terminal portion" of the polysaccharide. When American Cyanamid linked a protein to two

terminal ends, it still linked to "a terminal end" and infringed the claim. American Cyanamid indisputably always links at a terminal portion of the polysaccharide, but argues that the trial court correctly read "a terminal portion" to mean "a single terminal portion." The claims simply do not contain that limitation.

If the trial court had properly relied on the patent specification or prosecution history to construe the claims, it would have noted that these correct patent sources do not even mention "monofunctionality" or "monovalency." A comparison of the inventors' scientific writings with their later patent writings shows a complete deletion of all references to "monofunctionality" or "monovalency." Ironically, the scientific writings, in the proper context of the patent, show that the inventors—by deleting references to "monofunctionality"—clearly did not limit the claims to linkage at a single terminal end.

The panel's opinion recognizes the trial court's error in its extensive reliance on impermissible evidence. Nonetheless the panel compounds the error by creating on its own the same limitation. The panel purports to find this limitation in the specification.

In the first place, this court of appeals prohibits importation of limitations from the specification into the claims. *In re Lundberg*, 244 F.2d 543, 548, 123 USPQ 530, 534 (CCPA 1957). The panel's belated discovery of a limitation to a "linkage at only one terminal portion" in the specification should still not influence its reading of the claims. Slip Op. at 9, lines 17-18.

To my eyes, however, the specification does not contain anything close to the "only one terminal portion" limitation. As already noted, the specification never refers, even obliquely, to monofunctionality, i.e., linkage to a single terminal end. The panel perceives this monofunctionality in the singular references to terminal linkages and in a single example in the specification.

The singular references in the specification are an effort to preserve grammatical accuracy, not create a limitation. The specification adopts the same grammatical number as the terms in the claims. Because the claims discuss each terminal end separately, the specification does the same. Naturally, therefore, the specification uses the singular number. The specification does not demonstrate monofunctionality; rather, good grammar.

The specification's example from the meningococcal group of polysaccharides also does not create a limitation missing from the claims. This example discussed one element only of the Markush groups of claims 12 and 25. Monofunctionality in a single member of the Markush group does not mean all members of the group can only produce a single linkage. By narrowly construing the example and importing that construction into the claim, the panel in effect limits the patent to a single example in the specification. This single example simply does not, and should not, limit the entire claim.

A specification can supply understanding of unclear claim terms, but should never trump the clear meaning of claim terms. *E. I. Du Pont de Nemours & Co. v. Phillips Petroleum Co.*, 849 F.2d 1430, 1443, 7 USPQ2d 1129, 1131 (Fed. Cir. 1988). Moreover a specification should have a clear and distinct message before it influences claim meaning at all. In this case, the panel exalts the specification—without a single express reference to "monofunctionality" and without any unambiguous reference limiting linkages to a single terminal—over the express meaning of claim terms.

Not only did American Cyanamid literally infringe by linking to "a terminal portion," it chose precisely the polysaccharide mentioned in dependent claims 12 and 25—the polysaccharide of *H. influenza*. Moreover, the trial court found that the *H. influenza* polysaccharide links at more than one terminal end. Therefore, these dependent claims show that claim 11's language em-

braced each protein link "at a terminal portion." Not only does American Cyanamid literally infringe claim 11, it does so with precisely the polysaccharide in claims 12 and 25.

Claim 11—"without significant cross-linking"

Claim 11 also contains the phrase "without significant cross-linking." The term "cross-linking" could apply to three types of bonds: (1) the covalent bond between the protein and the polysaccharide polymers, (2) any linkage randomly located on the polysaccharide, and (3) a linkage at "a terminal portion of the polysaccharide" in the presence of another linkage. The claims exclude from the term "cross-linking" the type (1) bond because the claims call such a bond simply a "linkage". The specification includes the type (2) bond within "cross-linking." The Background section of the patent indicates that these random linkages along the polysaccharide were a problem in the prior art which the invention cures. Neither the claims nor the specification include the type (3) bond, linkage at "a terminal portion of the polysaccharide," within the realm of "significant cross-linking." In fact, the conspicuous absence of the terms "monofunctional", "monovalent", and their equivalents from the specification suggest that the type (3) bonds are not the "significant cross-links" which the invention sought to avoid.

Indisputably, the terms of the claim preclude the type (1) bond as the prohibited cross-link. The specification expressly discusses the random type (2) bonds as the cross-links which reduced the conjugant's benefit as an antigen in the prior art. The patent discussed "significant cross-linking" only in the context of avoiding the prior art problem with "many randomly activated functional groups . . . on the various polysaccharides leading to considerable cross-linking." *See* Col. 2, lines 14-18. The invention specifically sought to avoid this type of random cross-linking. For this reason the claim expressly forbid "significant cross-linking." Thus, according to the spe-

cification, the "significant cross-linking" prohibited by the claims refers to type (2) bonds.

Furthermore, the specification also points out that the invention permits a difference between reactivity along the group C polysaccharide chain and reactivity at a terminal end. *See* Col. 5, lines 50-54. These interchain linkages—the random type (2) bonds—display less reactivity than linkage at terminal ends. The inventors further explain that the interchain 2—8 linkages of the group B polysaccharide are even less likely to react under the conditions of the invention. *See,* Col. 5, lines 54-59. By noting this distinction, the specification reveals the inventors' intent to avoid interchain cross-links: Inexplicably the panel overlooks this additional evidence that the invention intended the "without significant cross-linking" limitation to mean type (2) interchain linkages, the inventors' term for linkages along the backbone of the polysaccharide.

In the face of this clear evidence of the meaning of "without significant cross-linking," the trial court found that the type (3) bond was the forbidden form of cross-link. Again the trial court's reliance on impermissible evidence caused this error. Based on this external evidence, the district court incorrectly decided that the claim embraced only monofunctional linkages.

The panel again embraces the decision reached by the trial court's clear error. In this case, however, the panel cannot draw credible support for its position from the specification. The patent specification clearly suggests that "without significant cross linking" refers to "many randomly activated functional groups" and not to cross-linking at a terminal portion of the polysaccharide.

More importantly, the panel overlooks the language of the claims. The claim language discusses linkage "at a terminal portion" specifically and then generally prohibits "significant cross-linking." The specific reference to

terminal portion linkage suggests that the general cross-linking language refers to something other than terminal portion linkage. Striving to justify its importation of monovalency into the claim terms, the panel construes "cross-linking" as the type (3) bond. In doing so, however, the panel disregards the language of the claims and the clear meaning of the specification.

Claim 25

Neither the trial court nor the panel adequately explains how the accused composition avoided infringement of claim 25. Even construing "without significant cross-linking" to mean "with absolutely no cross-linking," the accused product still infringes claim 25. Claim 25 uses open ended "comprising" terminology. The claim requires only that the vaccine contain a *component* which is (i) an *H. influenza* polysaccharide, (ii) antigenic with a molecular weight (M_w) above 2,000, (iii) a polysaccharide:protein coupled via -CH_2-N-protein linkage to "a terminal portion of the polysaccharide," and (iv) "without significant cross-linking." American Cyanamid's accused product contains a *component* which the trial court called a "monomer." Dr. Eby, Cyanamid's own expert witness, testified that 50% of the accused product was this "monomer" component. Both parties agree and the district court found that this monomer component is a non-cross-linked species of protein linked to polysaccharide. Therefore, this component is (i) an *H. influenza* polysaccharide, (ii) antigenic with a M_w above 2,000, (iii) a polysaccharide:protein coupled via -CH_2-N-protein linkage to "a terminal portion of the polysaccharide," and (iv) "without significant cross-linking." By the definition, this product with 50% infringing material infringes the open-ended claim 25.

American Cyanamid merely took a patent on A, B, C —(A) *H. influenza* polysaccharide (B) linked at a terminal portion to protein (C) without significant cross-

linking—and added a new element, D. The new element, D, is material ("dimers" and "trimers") linked at more than one terminal position. Adding some "dimers" to the infringing "monomer" material does not defeat infringement. Adding an additional component D does not defeat infringement of an open-ended claim to A, B, C. *Loctite Corp. v. Ultraseal, Ltd.*, 781 F.2d 861, 865, 228 USPQ 90, 92 (Fed. Cir. 1985) ("It is uncontested that Ultraseal's PC504 contains a monomer and an initiator selected from the monomers and initiators of the patent claims. Though PC504 also includes components not required by the claims, such inclusion does not avoid infringement. . . .") (footnote omitted); *Amstar Corp. v. Envirotech Corp.*, 730 F.2d 1476, 1484, 221 USPQ 649, 655 (Fed. Cir.), *cert. denied*, 469 U.S. 942 (1984); *A.B. Dick Co. v. Burroughs Corp.*, 713 F.2d 700, 703, 218 USPQ 965, 967 (Fed. Cir. 1983), *cert. denied*, 464 U.S. 1042 (1984) ("It is fundamental that the one cannot avoid infringement merely by adding elements if each element recited in the claims is found in the accused device").

Overlooking claim 25's language totally destroys the value of the patent. Potential infringers need only add an additional component, i.e., some "dimer" material, to avoid infringement. Thus, even adopting the trial court's strained interpretation of "conjugate," I would reverse the trial court's judgment of non-infringement on claim 25.

Conclusion

This claim is not ambiguous. It clearly requires only linkage "at a terminal portion." Nonetheless the Supreme Court's admonition applies here: "if the claim [is] fairly susceptible of two constructions, that should be adopted which will secure to the patentee his actual invention." *Smith v. Snow*, 294 U.S. 1, 14 (1935). The record also shows American Cyanamid could not create "[a]n antigenic-polysaccharide:protein conjugate wherein

the polysaccharide and protein are covalently linked through a CH_2-N-protein linkage to a terminal portion of a polysaccharide," until shortly after gaining access to the inventors' work. In the face of evidentiary errors by the trial court in conflict with the meaning of the claims, I would remand.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

93-1076

NORTH AMERICAN VACCINE, INC. and
NATIONAL RESEARCH COUNCIL OF CANADA,
Plaintiffs-Appellants,

v.

AMERICAN CYANAMID COMPANY and
PRAXIS BIOLOGICS, INC.,
Defendants-Appellees.

On Appeal from the United States District Court
Southern District of New York
in Case No(s). 91-CV-1449

JUDGMENT

This CAUSE having been heard and considered, it is ORDERED and ADJUDGED:

AFFIRMED-IN-PART AND REVERSED-IN-PART

DATED Oct. 6, 1993

ENTERED BY ORDER
OF THE COURT

/s/ Francis X. Gindhart
FRANCIS X. GINDHART
Clerk

Issued as a Mandate: December 15, 1993

UNITED STATES DISTRICT COURT
SOUTHERN DISTRICT OF NEW YORK

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91 Civ. 1449 (TPG)

NORTH AMERICAN VACCINE, INC., *et al.*,
Plaintiffs,

-against-

AMERICAN CYANAMID COMPANY, *et al.*,
Defendants.

OPINION

[1801] THE COURT: I'd like to now put my findings and conclusions on the record, and I do that with this preface:

This has obviously been a long and complicated case, and I'm sure that it might appear foolhardy to try to render a bench decision. But for me what is important is to make my ruling while I have in my mind, and fresh in my mind, the benefit of all the hard work that has gone on by the lawyers and all the rather vigorous interchanges that have gone on between me and the lawyers.

Now, I'm going to put down on the record with the court reporter my findings and conclusions.

After that, the parties can see the transcript, and if they have any feelings about something that is left out that hasn't been covered, they can request an amendment of the findings. But all that process will be over with, I would say, within a week, and I think a lot is to be gained by doing it this way.

I do not intend to discuss all the evidence. I do not intend to discuss the pros and cons and significance of even a substantial part of the evidence. What I am going

to do is to make my findings and my conclusions with some relatively brief explanation.

I have been furnished with legal authorities, both at the beginning of the trial and at various points through the trial, and I have considered the relevant [1802] authorities, although I do not intend to cite them specifically in this statement.

Now, let me repeat what I have indicated before, and that is that the case has been presented in the most remarkable manner. The skill and thoroughness and fairness and courtesy of all the participants have been an absolute model. The examination and cross-examination, all those things have done their job. It wasn't a wasted effort in any way.

And certain of the attorneys have been spokesmen for their clients, but obviously there has been a lot of very hard work by the staff that helped those attorneys, and all of that has produced a trial with very fine organization and elucidation of the subjects.

I think the case is a close one. That means that the plaintiffs have powerful points in their favor. Those points have been expressed with great weight by Mr. Diaz and his colleagues. The defendants have powerful arguments in their favor. Those arguments have been expressed by the attorneys for the defense.

The decision has to be made, and I believe that the scales tip, not drastically, but I think they tip in favor of the defense.

The case, of course, involves patent number 4,356,170. The application was filed May 27, 1981. It was [1803] issued October 26, 1982. The principal inventor is Harold J. Jennings of Ottawa, Canada. Also listed as an inventor is Mr. Czeslaw Lagowski.

The plaintiffs are North American Vaccine, Incorporated, and National Research Council of Canada. The suit is a claim for patent infringement. It is brought against American Cyanamid Company and Praxis Biologics, Inc.

The patent relates to certain technology involved in vaccines. Neither Dr. Jennings, nor the other inventor, nor the plaintiffs have actually produced a vaccine or any product based on the patent. However, Cyanamid and Praxis have produced a vaccine called HibTITER, which is intended to deal with a particular kind of meningitis. That vaccine is highly successful, and the claim is that that vaccine infringes certain claims of the '170 patent, specifically, claims 12 and 25.

The question which has been involved in most of the evidence and argument of this trial is the question of interpretation of claims 12 and 25.

I think it is safe to say that if claims 12 and 25 were to be interpreted in accordance with plaintiffs' position here, it would not be difficult to find infringement.

So the basic question upon which the infringement issues depend is how should we interpret claims 12 and 25. [1804] Since this is an infringement case, and the plaintiffs have the burden of proof on infringement, I believe it is safe to say they have the burden of proof to show their particular interpretation, as that is foundational to the infringement issue.

Now, claim 12 and claim 25 are both dependent upon claim 11, and it is necessary to read into the record claim 11, which is as follows:

"An antigenic-polysaccharide:protein conjugate wherein the polysaccharide and protein are covalently linked through a CH2-HN-protein linkage to a terminal portion of the polysaccharide without significant crosslinking, said antigenic polysaccharide having a MW above about 2,000."

Now, claim 12 reads as follows:

"The conjugate of claim 11 wherein the antigenic polysaccharide is selected from the group derived from meningococci, Haemophilus influenza, pneumococci, B-hemolytic, streptococci, and E. coli."

Claim 25 reads as follows:

"A human infant vaccine comprising the conjugate of claim 11 wherein the polysaccharide comprises at least one of meningococcal polysaccharide and Haemophilus influenza polysaccharide."

Now, although claim 11 is not literally referred to in the infringement cause of action, it is foundational [1805] and its interpretation is crucial to a resolution of this case.

There are several issues about the meaning of claim 11. One is what is meant by the word "conjugate". I'll come back to that later. The most serious issue relates to the phrase "a terminal portion of the polysaccharide without significant crosslinking." The phrase "a terminal portion" is, of course, in the singular.

The defense contends that this singular phrase should be interpreted as just that: as providing for linkage at one terminal portion of the polysaccharide. This is a crucial point because the vaccine produced and marketed by defendants involves the use of polysaccharides, which have linkages at both terminal portions at both ends.

A polysaccharide can be viewed as being a string. A string has two ends. HibTITER has the chemical linkage at each end, at both ends, at both terminal portions. Thus, it is crucial to defendant's case to urge upon the Court that the language in claim 11 should mean literally what it says: that it is a claim in which there is to be linkage at one terminal portion of the polysaccharide, not at both ends, not at each end.

There was extensive evidence at the trial about the background of Dr. Jennings' invention, the technology which existed at the time of his invention, the problems in [1806] the immunization of people who were sought to be immunized against certain diseases.

The polysaccharide was known to be important in creating the kind of vaccines that Dr. Jennings and other scientists were working on. There were various problems in the use of these polysaccaharides. One of these prob-

lems was the question of how the polysaccharide would be introduced into the system of the person being vaccinated or immunized, and the focus of the particular work was upon infants, very small infants.

Their needs as far as immunization were different from older children and from adults, and the evidence in this case indicates that one way, and perhaps the only way, but at least one way of getting the polysaccharide introduced into the system of the infant was to have it linked to a protein, or perhaps more than one protein, and the protein would carry out the job of getting it into the system of the infant. And that is why claim 11 talks about linking a protein to a polysaccharide.

Now, some of the work in this field involved methods which placed a great deal of protein matter on the polysaccharide, that protein matter being distributed all along the length of the polysaccharide. The problem with this was that there was too little polysaccharide left exposed, and I think the evidence refers to this problem as [1807] being that the immune system of the infant would not recognize the polysaccharide. In any event, covering the polysaccharide with protein or having a lot of protein along the length was a problem.

As we know from the evidence in this case, that which I have just called a problem perhaps was not perceived by everyone as a problem, because certain parties developed products in which this situation occurred where there was protein distributed along the length of the polysaccharide. But at least to some scientists it was viewed as a problem, and certainly it was viewed as a problem by Dr. Jennings.

If we just stepped away from the chronology of the developments and thought in an abstract way, we might say that the issue of having protein distributed along the length of the polysaccharide might be solved if the protein were placed at one end of the polysaccharide, or, in the language of claim 11, at a terminal portion of the polysaccharide.

Again, speaking somewhat abstractly, one might say that the problem of having protein distributed along the length of the polysaccharide might be solved by having protein distributed at the two ends, the two terminal portions, provided that the portion was not massive or the polysaccharide was not so short that this somehow obscured the polysaccharide.

[1808] But given proper proportions of the polysaccharide and protein, it is not difficult to conceive of the issue under discussion as being taken care of by a polysaccharide having a protein at one end or having a protein at two ends.

Now, it is time to mention the issue of crosslinking. Crosslinking refers to a situation where a polysaccharide acts as a link between two proteins. If proteins are located all along the length of a polysaccharide, there are many crosslinks. Each space on a polysaccharide between two proteins is a crosslink.

There are other ways in which crosslinking can come about creating structures that look like networks. This results in what some perceive as a problem in defining the exact structure.

If there is a great deal of crosslinking and different kinds of networks, the definition of the substance, the definition of the molecular shape becomes more and more vague and more and more diffuse. Crosslinking also affects the solubility. The more crosslinking, the less solubility.

It is a fact established in the evidence that where a polysaccharide has a protein linked at one end, there is no crosslinking. You can have several polysaccharides linked to one protein, but none of those [1809] polysaccharides are linked to two proteins, and thus there is no crosslinking.

When you have polysaccharides with protein all along the backbones, there is abundant crosslinking. Where you have polysaccharides with proteins at the two terminal ends, there is less crosslinking than in the situation just

mentioned, but there still will develop, as illustrated in the evidence in this case, a substantial amount of cross-linking.

Now we come back to the question of interpretation. Plaintiffs contend that the singular phrase "a terminal portion of the polysaccharide" is a kind of generic term and it is not intended and should not be interpreted to be limited to one single terminal portion. It should be interpreted to refer to a terminal portion at one end and also a terminal portion at the other end where there is such a thing.

In effect, plaintiffs wish to have the claim 11 language interpreted to mean a terminal portion of the polysaccharide at one or both ends.

As I have indicated, the defense position is that the claim 11 language means what it says, and refers only to a single terminal portion.

Now, as I've said many times during the trial, we cannot solve this problem by staring at the language and [1810] simply saying there is a singular indefinite article and a singular noun and that is that. It is perfectly possible, as an initial proposition, that the phrase "a terminal portion" is a generic term and could mean exactly what plaintiffs say it means.

In order to solve the problem, we need to look at some of the other evidence that can be considered properly under the law on the question of interpretation. We, of course, need to look at the other portions of the patent: the summary of the invention; the description of the experiments; other claims besides 11, 12 and 25. In other words, the whole patent.

In addition, there has been the testimony by the inventor, Dr. Jennings, and there has been discussed in the evidence at great length an article Dr. Jennings wrote in 1981 which was given by him to the drafter of the patent. That is Defendants' Exhibit F. Also referred to in our discussion of the case is a talk given by Dr. Jennings at the National Institute of Health in the fall of 1980, which

talk was embodied in an article which came out in 1982. This article is Defendants' Exhibit CT.

There is various other evidence relevant to the question of interpretation, including lengthy testimony by an expert called by plaintiffs, Dr. Harry Schoolnik of Stanford. I will not try to name all the witnesses, I will [1811] not try to sumarize all their testimony, but there has been a substantial amount of testimony and documents received into evidence bearing on the question of interpretation.

Perhaps the most important point in the evidence is the fact which is established without question, that is, that the laboratory work carried out by Dr. Jennings leading up to the patent was specifically designed to produce polysaccharides with protein linkage at only one end of the polysaccharide, that is, at one single terminal portion. [1812] In this work, it was not a matter of indifference to him whether one or two terminal portions were involved.

The testimony of Dr. Jennings, particularly on cross-examination, involved admission after admission about his desire in his experimentation to achieve what he called monofunctionality, which is another word for having the linkage at one end of the polysaccharide. He explained that he was doing this as a chemist, and he wanted a clear-cut chemical solution to the issues which I mentioned earlier. He wanted the clearest possible definition for the substance that he was creating. And therefore, he conducted experiments with the desire and the purpose of producing monofunctionality, that is, linkage at one terminal portion. This meant that cross-linking would be entirely avoided.

The only exception to this was that he knew that he might not be able to avoid some cross-linking because of some attachment of proteins at places other than the one terminal end, but this was something that would not come about by design, but only because in the world of chemistry, absolute purity might not be achieved. But he

sought, as he has admitted, the monofunctionality, which gave the best definition for the substance since it did not involve cross-linking.

This was made clear in his National Institute of Health speech and in the article he wrote in 1981. The [1813] speech and the article presented essentially the same concepts, described essentially the same experiments and described the same goals. For instance, in the article, he states as follows: "We have tried to extend the monofunctional group approach used in conjugating oligosaccharides to the larger molecular size meningococcal polysaccharides."

Later in the same article he states, "The ideal situation would be to specifically introduce one of these functional groups per polysaccharide molecule, preferably located in a terminal position."

Still later in the same article, he talks about monovalent polysaccaride molecules.

Let me say that were he speaks of functional groups, what is being talked about is a group not in the sense of one protein linked at one end and another linked at another end. But the group is a reference to a group of atoms, hydrogen, oxygen, and carbon.

Another expression that has been used at the trial is the word aldehyde, again referring to this grouping of the hydrogen, oxygen, and carbon atoms.

Now, there is simply no question about the fact that if the language of the 1981 article and of the NIH speech had been literally carried over into the patent, we really would have no issue here. It would be crystal clear [1814] that the patent related to monofunctionality. That is the idea of the linkage being at the one terminal portion of the polysaccharide. There really would be no problem with interpretation that anybody could sensibly raise.

However, the patent does not carry over the literal language of the NIH speech or the 1981 article. It does not use the word monofunctionality. It does not use the word monovalence. It does not literally say that Jennings is

trying to achieve one functional group. However, on some crucial points, certain language of the article and of the NIH speech are carried over into the patent and what has occurred is something which is rather odd in light of plaintiffs' contentions and Jennings's testimony here.

Jennings testified that when it came to taking out his patent, he intended to claim something broader than what he talked about in his speech and his article. He has testified that he did not intend his patent to be limited to monofunctionality. He has testified that his intent was to cover where the terminal linkage occurred at both ends of the polysaccharide.

Now it is clear that in the article and the speech, he was not talking about terminal portions at two ends, or what we call difunctionality. But he says when it came to drafting the patent, he intended to have his patent [1815] drafter broaden out his claims to cover the two terminal end situations.

And as already stated, he points to the fact that the word monofunctional and the word monovalent, those words are not present in the patent. The problem is that in some crucial respects, although he has left out those particular words, he has carried over other descriptive wording which was in the article and the speech which were tied in with the use of those words, monofunctional and monovalent. Thus, in the patent, those particular words are left out, but the descriptions which develop the concept of monofunctionality are carried over into the patent.

An example of this, I think, is worth reading, and I will do so. On page 1012 of the article he states, "We have tried to extend the monofunctional group approach used in conjugating oligosaccharides to the larger molecular size meningococcal polysaccharides. This was achieved by the introduction of a terminally located free aldehyde group into the polysaccharide molecules through which they could be specifically coupled to protein without activating the other functional groups on the poly-

saccharide. This procedure avoids cross-linking, minimizes the possibility of extraneous chemical modification of the polysaccharides, and results in better-defined immunogens."

Now, in the summary of the invention in [1816] the patent, we have wording which is very, very close to the wording in that article and contains most of the language which was obviously designed in the article to convey and elaborate upon the monofunctional approach. However, in the patent, and the language I will just read now, the word monofunctional is not there.

Thus, the patent states, and I'm reading from column 2, beginning at line 33: "We have found it possible to introduce a free aldehyde group into the polysaccharide molecule in a terminal location and to specifically couple this aldehyde group to protein without activating other functional groups on the polysaccharide. This procedure avoids cross-linking and extraneous chemical modification of the bulk of the polysaccharide resulting in better-defined immunogens."

Now, that language, in substance, and almost verbatim form, was in the article. Obviously in the article it was inexorably linked to the concept of monofunctionality. However, in the patent, although the word monofunctional was omitted, the attending language, which was an elaboration of the monofunctional idea, was carried over into the patent.

Now, anyone reading the patent will find over and over again references which talk about the single terminal group. I don't think the word single is used, but the [1817] singular usage is over and over again presented. I don't think any purpose would be served in reading all those references; but let me just set down a few of them.

The first two lines of the patent refer to a terminally located aldehyde group. That, of course, is in the singular, and as I have stated, group does not talk about linkage at two ends. It talks about a group consisting of three types of atoms. Sometimes instead of saying alde-

hyde group, we say aldehyde. It is in the singular. In column 2, line 61, there is a reference to linkage to a terminal portion. That language forecasts the language of claim 11. Column 3 refers to a terminal portion of the molecule. And of course, we come to claim 11, which has that same language, a terminal portion of the polysaccharide. There are many other references which can be easily found with the same kind of wording.

Thus, again, what happened was that the concept of the speech and article was carried over into the patent. It is true that words such as "monofunctional" were not there, but all the other attendant wording is there.

Now, the question naturally presents itself. If Dr. Jennings sought to broaden his patent beyond what was contained in the article and the speech, why did he not express this intention? If his intention was to have a patent on the production of aldehydes at both terminal ends, [1818] this is something that can be easily expressed in the English language, and clearly expressed. If he desired to depart from the objectives that he so clearly had in his experimentation described in his article and his speech, if that was his purpose, surely that was something that he thought about, it wasn't just chance, and he would want to think about how to express it.

He did not express it. And that is the basic reason why I am holding in favor of the defendants on the question of interpretation. There are ample means through simple devices of wording to convey what he claims was his intention. He simply did not do it.

My ruling is that the wording in claim 11, "a terminal portion," should be interpreted to refer to monofunctionality, and that is the way I am interpreting it.

Now, we come to the phrase "without significant cross-linking." There is some indication in plaintiffs' arguments that there was an intention along with incorporating this difunctional approach into the patent to provide for cross-linking because it has certain legitimate chemical benefits, although it does indeed have some detriments.

But there is nothing in this patent affirmatively teaching anything about achieving cross-linking. There is nothing in the patent except a negative view of [1819] cross-linking.

The proper interpretation is that the phrase "without significant cross-linking" was inserted simply to cover the possibility that I've earlier described, that in the chemical process, one cannot be assured of absolute purity, there may be some cleavage and some proteins appearing in places that were not intended, and the patent is designed to cover that situation.

This brings us to the final point about claim 11, and that is what is meant by the word "conjugate." Plaintiff contends that conjugate refers to the molecule itself. The defense contends that it refers to the mixture consisting of the various molecules which are produced. Conjugate is referred to many times in the patent. Judging from the patent as a whole, it is quite clear that conjugate in claim 11 means the mixture and not the single molecule. This is also made clear by the testimony of Dr. Jennings himself.

On the overall issue of interpretation, plaintiffs' expert witness, Dr. Schoolnik, gave very interesting testimony. He testified that if he looked at the language of the patent and the background that I've described, he would say that it only covered monofunctionality. And the only reason he could voice an opinion in favor of difunctionality —that is, covering the [1820] production of two terminal linkages at the two ends of the polysaccharide—was that there is a reference in the claims 12 and 25 and one or two references in the other portions of the patent to Haemophilus influenza. He said that the Haemophilus influenza polysaccharide, at least the one that was best known in this field of technology, would necessarily yield aldehydes at the two ends. And therefore, this reference in claim 12 and claim 25 and one or two other places drives the interpretation of the entire patent so that claim 11 covers, the whole patent covers one or both terminal

portions. It covers monofunctionality and it covers difunctionality.

I really cannot accept this proposed method of interpretation. This patent has a great deal of discussion of experimentation and theory, and it is all referring to this monofunctional approach. To allow all of that weight, really massive weight of discussion, descriptions of experiments and so forth, to be cancelled out by the two words "Haemophilus influenza," in my mind, would not be a fair method of interpretation.

Other points need to be made about claims 12 and 25. Claim 12 refers to five different groups or families of bacteria with polysaccharides. And each of those families has numerous, what are called serotypes. It has been stipulated that if the Jennings oxidation process were [1821] applied to all of these serotypes of the five groups referred to in claim 12, some would produce a monofunctional result. Some would produce a difunctional result. Some would produce a polyfunctional result; that is, protein distributed all along the polysaccharide.

And I think it is clear from the record that on some of these serotypes, it is not known what would happen. In addition, it is stipulated that on some of these serotypes which would not naturally and easily yield the monofunctional result, such a result could be obtained if there was pretreatment of the kind taught at an earlier point in the patent.

Now, as for Haemophilus influenza, this is a family or group which has five or six serotypes. Haemophilus influenza B is the one which yields the difunctional result if the Jennings type oxidation is used and if it is controlled in a way which is appropriate to Haemophilus influenza.

Plaintiffs admit that much of what is referred to in claim 12 would not be appropriate for the Jennings patent, that is, the situations where proteins are distributed all along the backbone, the polyfunctional result. Plaintiffs deal with this by saying that these situations should be read out of claim 12. They should be rejected, ignored.

[1822] The question is: What do you do with Haemophilus influenza B? In my view, the same thing should be done about Haemophilus influenza, as with the polyfunctional polysaccarides. The question should be: What is the main teaching of the patent? Does the patent, prior to claim 12, teach a difunctional result? Claim 12 and also claim 25 derive from claim 11, and obviously stem from the whole body of the descriptive material in the patent. In my view, it is improper to ignore that in respect of Haemophilus influenza any more than for the serotypes where polyfunctionality occurs. Difunctionality is simply not taught by the bulk of the descriptive material in this patent. It's not specifically taught in claim 12 or claim 25. All that we have is some alleged implication of a difunctional result resulting from the phrase Haemophilus influenza, allegedly known to scientists who know the necessary chemistry. This is far from teaching difunctionality in clear language in a patent.

There has been an argument that claims 12 and 25 are invalid because there are so many different kinds of polysaccharides referred to which would yield different results. Polyfunctional, difunctional and monofunctional, some of which results are admittedly contrary to the patent's teaching.

In other words, the contention of the defense is [1823] that claims 12 and 25 are invalid because they really don't teach anything that is definite, or define anything that is sufficiently definite in accordance with Section 112 of the patent law. I agree with that contention, and I hold that claim 12 and claim 25 are both invalid on the ground asserted by the defense. In the alternative, even if they are to be deemed valid, I hold that there is nothing in either claim which can be properly interpreted to define a difunctional result contrary to claim 11 and the teaching of the patent as a whole.

[1824] What I have ruled as far as the interpretation issues dictates the result of the infringement claim. Since the proper interpretation of the patent, including claims

12 and 25, is to define a monofunctional substance, defendants' product HibTITER cannot be held to infringe because it involves a difunctional substance.

Plaintiffs have one alternative argument about infringement which must be dealt with. They contend that even if defendants prevail on their basic interpretation arguments, still there is infringement. They contend that there is in HibTITER a certain amount of monofunctionality involved in the so-called monomers which constitute a portion of the molecules in the product.

This argument largely depends on the meaning of the word "conjugate" in claim 11. They urge that "conjugate" refers to the molecule, so a single molecule could be an infringing molecule. I reject that interpretation, as I have said, and have ruled that "conjugate" refers to the mixture.

But even as to the individual molecules, there is no showing that the HibTITER contains any truly monofunctional polysaccharides. Defendents' process creates cleavage through oxidation. The polysaccharide fragments which result have aldehydes at each of the two ends.

There are situations, apparently, where only one [1825] of those aldehydes links up to a protein, and indeed there apparently are many of those situations. But this is not because they do not have an aldehyde created at both ends. It is because, by chance, only one aldehyde links with a protein and, in a further portion of the chemical process, the other end becomes capped.

But more importantly, "conjugate" refers to a mixture, and the mixture, in order to be within claim 11, and therefore, within claims 12 and 25, must be without significant crosslinking. The evidence is overwhelming that the mixture involved in HibTITER has very substantial crosslinking.

A high proportion of the molecules are what are called dimers or trimers, and these molecules involve crosslinking to a significant degree. Therefore, there is no

infringement even on this alternative theory suggested by plaintiffs.

For the above reasons plaintiffs' complaint is dismissed.

And so that concludes our proceedings. Thank you.

MR. DIAZ: Thank you very much, your Honor.

MR. THOMASCH: One housekeeping matter, your Honor. Am I right that we should collect back our exhibits from the Court?

[1826] THE COURT: Well, I want to keep what I have on the bench.

MR. THOMASCH: All right. There's only—

THE COURT: Everything out here.

MR. THOMASCH: I think there's one confidential exhibit. We would just ask that that not be publicly filed.

THE COURT: I'll watch that.

MR. THOMASCH: Thank you, your Honor.

(Proceeding adjourned at 2:25 p.m.)

SO ORDERED.

Dated: New York, New York
September 9, 1992

/s/ Thomas P. Griesa
THOMAS P. GRIESA
U.S.D.J.

UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

93-1076

NORTH AMERICAN VACCINE, INC. and
NATIONAL RESEARCH COUNCIL OF CANADA,
Plaintiffs-Appellants,

v.

AMERICAN CYANAMID COMPANY and
PRAXIS BIOLOGICS, INC.,
Defendants-Appellees.

ORDER

[Filed Dec. 8, 1993]

A combined petition for rehearing and suggestion for rehearing in banc having been filed by the APPELLANT, and a response thereto having been invited by the court and filed by the APPELLEE, and the petition for rehearing having been referred to the panel that heard the appeal, and thereafter the suggestion for rehearing in banc and response having been referred to the circuit judges who are in regular active service,

UPON CONSIDERATION THEREOF, it is

ORDERED that the petition for rehearing be, and the same hereby is, DENIED and it is further

ORDERED that the suggestion for rehearing in banc be, and the same hereby is, DECLINED.

The mandate of the court will issue on December 15, 1993.

FOR THE COURT,
FRANCIS X. GINDHART
Clerk

By /s/ Diane M. Frye
DIANE M. FRYE
Chief Deputy Clerk

Dated: December 8, 1993

cc: JOHN A. DIAZ
DONALD R. DUNNER

Supreme Court, U.S.
FILED
APR - 6 1994
OFFICE OF THE CLERK

No. 93-1385

IN THE

SUPREME COURT OF THE UNITED STATES

OCTOBER TERM, 1993

NORTH AMERICAN VACCINE, INC. and
NATIONAL RESEARCH COUNCIL OF CANADA,
Petitioners,

v.

AMERICAN CYANAMID COMPANY and
PRAXIS BIOLOGICS, INC.,
Respondents.

ON PETITION FOR A WRIT OF CERTIORARI TO
THE UNITED STATES COURT OF APPEALS
FOR THE FEDERAL CIRCUIT

RESPONDENTS' BRIEF IN OPPOSITION

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April 6, 1994

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COUNTER-STATEMENT OF THE QUESTION PRESENTED

Whether the U.S. Court of Appeals for the Federal Circuit properly affirmed a judgment of noninfringement based on an issue of claim interpretation, after ruling that the district court erred in relying on certain evidence, where:

(a) petitioners asked the Federal Circuit to review the district court's claim interpretation *de novo* and to construe the claims as a matter of law,

(b) the Federal Circuit relied upon undisputed facts and conclusions of law to interpret the claims, and

(c) the district court almost certainly would have reached the same claim interpretation even without the alleged error.

STATEMENT PURSUANT TO RULE 29.1

The parents, subsidiaries and affiliates of Respondents American Cyanamid Company and Praxis Biologics, Inc., other than those that are wholly owned, are listed below:

AC Molding Compounds

American Melamine Industries (a partnership)

Biotechnology Research and Development Corporation
(Consortium consisting of the following companies owning 400 shares of common stock:
Agricultural Research and Development Corp.
American Cyanamid Company
Amoco Technology Company
Imcera Group, Inc.
Dow Elanco
Hewlett-Packard Company
Ecogen, Inc.)

B. Braun-Dexon GmbH

B. Braun Melsungen AG)

B. Braun-Dexon (Portugal) Produtos Hospitalares Limitada

B. Braun-Dexon, S.A.

Criterion Catalyst Canada Inc.

Criterion Catalyst Company

Criterion Catalyst Company L.P. (a limited partnership)

Cyanamid India Limited

Cyanamid Italia S.p.A.

Cyanamid (Pakistan) Limited

Cyanamid Taiwan Corporation

CYRO Canada Inc.

CYRO Industries (a Partnership)

Dyno Cyanamid B.V.

Dyno Cyanamid C.V.

Dyno Cyanamid K.S.

Esterfarm Laboratori Farmaceutici S.r.l.

Eximp, S.A.

Irbi, S.p.A.

Laboratorios Sobrino S.A.

Laminate Industries (Proprietary) Limited

Lederle (Japan), Ltd.

Lederle (Nigeria) Limited

Mitsui-Cyanamid, Ltd.

Productora-Distribuidora Sobrino, S.A.

Sutumex, S.A. de C.V.

Suzhou Lederle Pharmaceutical Company Ltd.

Takeda Italia Farmaceutici S.p.A.

YuHan-Cyanamid, Inc.

Miscellaneous Minor Equity Investments:

Company

American Casualty Excess Insurance Company, Ltd.

Applied Microbiology Inc.

California Laboratories Inc.

Corporate Officers and Directors Assurance, Ltd. (CODA)

Cortecs Limited

Credence Investment and Finance Pvt. Ltd.

Cyanotech Corporation

Dallas Investment and Trading Co. Pvt. Ltd.

Delta Holdings, Inc.

Ecogen Inc.

Embrex Inc.

EXEL Limited

Hopewell International Insurance Limited

ImClone Systems, Inc.

Inmunologia Y Genetica Aplicada, S.A.

Ingenasa

IRE Celltarg

MGI Pharma, Inc.

Molecular Genetics, Inc.

Quadra Logic Technologies, Inc.

Senorita Investment and Trading Co. Pvt. Ltd.

Sepracor, Inc.

Societe Exploitation et Recherche Chirurgicales Lederle

Techniclone International Corp.

United Insurance Company

Uresil, L.P. (a partnership)

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RESPONDENTS' BRIEF IN OPPOSITION

COUNTER-STATEMENT OF THE CASE

Introduction

In this patent infringement action, tried to the bench, the dispositive issue involved interpreting the meaning of claim language. Petitioners allege that the Federal Circuit improperly affirmed the judgment because, in the course of interpreting the claims, it ruled that the district court should not have relied on certain evidence. Before the Federal Circuit, however, petitioners argued that claim interpretation in this case was an "issue of law" for the

court to decide "*de novo.*" Having urged that position before the Federal Circuit, petitioners are estopped from reversing positions now and arguing that the Federal Circuit erred by interpreting the claims itself rather than remanding to the district court.

Moreover, when interpreting the claims, the Federal Circuit did not engage in fact finding. The Federal Circuit concluded that the claims could be interpreted by relying on the claim language and the descriptions in the patent. Petitioners' testimonial evidence for an expansive interpretation, testimony that the Federal Circuit rejected on legal grounds, did not raise disputed factual issues requiring remand.

Furthermore, after reviewing the evidence, the Federal Circuit properly concluded that the district court's alleged error was "harmless." Petitioners attempt to convince this Court otherwise by misrepresenting the district court's reliance on the alleged error and by citing to the district court's courteous but perfunctory remarks at the beginning of its opinion that the case was "a close one." A careful review of the trial evidence, the district court opinion, and the Federal Circuit opinion, however, reveals that the district court almost certainly would have reached the same claim interpretation even without the alleged error. Thus, the alleged error did not "substantially influence" the district court and certainly does not warrant expending further judicial resources on either this petition or a remand.

In any event, this case raises only issues peculiar to its own facts and proceedings. Thus, this case does not warrant a writ of certiorari.

The Patent in Suit

The patent in suit covers certain "conjugate" vaccines, which are made of billions of polysaccharide molecules, each of which is linked to a protein. In essence, the patented invention covers a product made by a two-step process to link protein to the polysaccharide, which would not occur naturally. First, the polysaccharide must be treated to create a reactive site (called "an aldehyde group") at a terminal location, i.e., at the end of the polysaccharide. Second, the activated polysaccharide is chemically combined with a selected protein. In the resulting conjugate, only one protein is linked to a polysaccharide and crosslinking, which is defined as two or more proteins linked by a polysaccharide, is thus avoided.

Petitioners, the patent owner and exclusive licensee, asserted claims 12 and 25 of their patent against respondents. Both of the asserted claims are dependent upon claim 11, which reads:

> 11. An antigenic-polysaccharide:protein conjugate wherein the polysaccharide and protein are covalently linked through a
>
> $$-CH_2-\overset{H}{N}-\text{protein}$$
>
> linkage to a terminal portion of the polysaccharide without significant cross-linking, said antigenic polysaccharide having a [molecular weight] above about 2000.

The infringement issue raised by this petition focused upon the meaning of the phrase "linkage to a terminal portion of the polysaccharide without significant crosslinking" in claim 11.

The "summary of the invention" in the patent begins by describing the formation of the protein linkage to a terminal portion of the polysaccharide as follows:

> We have found it possible to introduce a free aldehyde group into the polysaccharide molecule in a terminal location and to specifically couple this aldehyde group to protein without activating other functional groups on the polysaccharide.

(2a, col. 2, lines 33-37).[1] This sentence refers to the protein linkage in singular terms, using the phrases "a free aldehyde group," "this aldehyde group," and "in a terminal location."

Throughout its text, the patent refers to the linkage between the protein and polysaccharide in singular terms. At no point does the patent teach that the inventors contemplated creating more than one reactive site on the polysaccharide (such as by use of the phrase "at least one") or linking the polysaccharide to more than one protein. When describing other aspects of their invention, however, the inventors used the conventional phrase "at least one" when they contemplated more than one (*see, e.g.*, 5a-6a, claims 22, 23 and 25).

The patent teaches that crosslinking (as would occur with polysaccharides having two or more active sites)[2] is a structural characteristic to be avoided (*see, e.g.*, 2a-3a,

---

[1] Citations preceded by "Pet. at _a," are to the Appendix to the Petition for a Writ of Certiorari; citations preceded by the letter designation "_a" are to the appendix to the Respondents' Brief in Opposition.

[2] Polysaccharides activated at one end are sometimes referred to as "monofunctional." Polysaccharides activiated at both ends are sometimes referred to as a "difunctional." Polysaccharides having more than two reactive sites are sometimes referred to as "polyfunctional."

col. 2, lines 37-39 and 62-63; 5a, col. 3, lines 62-63). Nowhere in the specification is crosslinking of any type identified as a desirable, or even an acceptable, aspect of the invention. Crosslinking is prevented by a single terminal linkage, i.e., monofunctionality.

No vaccine produced in accordance with petitioners' patent has been approved for sale in either the United States or abroad (18a-20a).

HibTITER

The accused product, HibTITER, is a vaccine against *Haemophilus influenza* type b ("Hib") bacteria, one of the leading causes of childhood meningitis. HibTITER was developed independently of petitioners' patent by Praxis Biologics, a subsidiary of American Cyanamid (21a-23a). HibTITER was the first vaccine against Hib bacteria approved by the FDA for use in young children (24a). Since HibTITER's approval, vaccinating children against Hib bacteria has become standard pediatric practice, and the incidence of meningitis caused by Hib bacteria has declined markedly (24a-25a).

HibTITER is made by linking proteins to difunctional Hib polysaccharide (fragments having reactive sites at each end of the fragment) (25a-26a). Because the Hib polysaccharide fragments have two reactive sites, each can link to a different protein, thereby producing crosslinked conjugates (27a-28a).

The Trial

From the outset of the trial, petitioners avoided the actual words of the patent and introduced new and

broader terms. For example, petitioners urged in their opening statement:

> [T]he '170 patent solves [the problem] by just making polysaccharide chains which have free aldehyde groups, single terminal aldehyde groups on one end or on both ends . . . .

(7a). Nowhere did the patent state that aldehyde groups could be formed "on one or both ends" of the polysaccharide.

Petitioners, however, urged that their expansive interpretation of the claims followed from the patent's "summary of the invention," the experiments reported in the patent, and the mention of *Haemophilus influenza* polysaccharide in claim 12. As a result, much of the trial focused upon whether these disclosures supported petitioners' argument. Petitioners' evidence in support of their argument consisted of the testimony of Dr. Harold Jennings, one of the inventors, and Dr. Gary Schoolnik, a retained expert witness.

Dr. Jennings testified what he "intended" the patent disclosure and claims to mean. Dr. Jennings testified that he intended the language "linkage to a terminal portion of the polysaccharide" to include protein linkages at both ends of the polysaccharide, contending "this can be read from the difference between my publications and . . . the patent, in which we do allow for crosslinking" (17a). Dr. Jennings testified also that he did not intend the "summary of the invention" or the description of his experiments in his patent to suggest that his invention was limited to linkages at a single terminal portion of the polysaccharide (16a-17a).

On cross-examination, respondents challenged Dr. Jennings's self-serving characterization of his patent, using

in part a 1980 NIH speech and 1981 article authored by Dr. Jennings which reported on the same experiments described in the patent (20a). Indeed, Dr. Jennings gave the 1981 article to his attorney, who used the article as a basis for drafting the patent (14a). Both refuted Dr. Jennings's direct testimony that it was a matter of indifference to him in his patent whether protein linked to one or both ends of the polysaccharide. Thus, respondents used the speech and article to rebut Dr. Jennings's after-the-fact characterization of his patent and his statements as to his intended meaning.

Dr. Schoolnik's testimony centered on the patent's mention of *Haemophilus influenza*, along with several other types of polysaccharides, in claim 12. Petitioners argued this reference to *Haemophilus influenza* meant the claims must cover linkages to both terminal portions of the polysaccharide. Dr. Schoolnik conceded that "my entire interpretation of the language where it is singular is driven by the specific examples of polysaccharides in claim 12 . . . ." (12a-14a).

However, on cross-examination, Dr. Schoolnik admitted that a number of other polysaccharides in claim 12 were polyfunctional and would form multiple linkages along the backbone of the polysaccharide. Dr. Schoolnik further admitted that such polysaccharides would not fall within the language of claim 11 (11a-12a). Thus, Dr. Schoolnik's position was reduced to an argument that one polysaccharide mentioned in claim 12 (*Haemophilus influenza*) should be used to construe the meaning of claim 11, while other polysaccharides mentioned in claim 12 should be ignored (8a-10a). Dr. Schoolnik could offer no explanation as to why *Haemophilus influenza* should be singled out of claim 12, rationalizing only

that "I'm not that concerned about the other polysaccharides [in claim 12]" (8a-9a).

The District Court Opinion

Following closing arguments, the district court dictated a 26-page opinion.

At the outset, the court complemented counsel for their trial presentation and politely remarked that the "case is a close one." The court then proceeded to reject every shred of evidence offered by petitioners as demonstrating a broader than normal meaning of the disputed claim language. At no point in the opinion did the court again suggest that the case was "close." Indeed, the court did not even consider it necessary to rely on respondents' affirmative evidence on the issue of claim interpretation.

The court began its analysis of the phrase "a terminal portion of the polysaccharide without significant cross-linking" by focusing on the language itself, explaining that "[t]he phrase 'a terminal portion' is, of course, in the singular." (Pet. at 31a). The court noted that petitioners wished to interpret the language to mean "a terminal portion of the polysaccharide at one or both ends," while respondents urged that the claim language "means what it says, and refers only to a single terminal portion." (Pet. at 34a).

The court then proceeded to assess petitioners' argument that the phrase should be interpreted differently than its ordinary meaning. The court set the framework for this inquiry as follows:

> [W]e need to look at some of the other evidence that can be considered properly under the law on the question of interpretation. We, of course, need to look at the other portions of the patent:

> the summary of the invention; the description of the experiments, other claims besides 11, 12 and 25. In other words, the whole patent.

(Pet. at 34a). Thus, the district court focused on the disclosures in the patent, especially the "summary of the invention" and the experiments. The court also considered the testimony of Dr. Jennings and Dr. Schoolnik.

The district court viewed "the most important point in the evidence" to be that "the laboratory work carried out by Dr. Jennings leading up to the patent was specifically designed to produce polysaccharides with protein linkage at only one end of the polysaccharide." (Pet. at 35a). The court noted that Dr. Jennings "conducted experiments with the desire and purpose of producing monofunctionality, that is, linkage at one terminal portion." *Id.*

The court rejected Dr. Jennings's testimony that "when it came to taking out his patent, he intended to claim something broader than what he talked about in his speech and his article," finding instead that "the descriptions which develop the concept of monofunctionality are carried over into the patent." (Pet. at 37a-38a). In particular, the court pointed to the patent's "summary of the invention," which employed wording "very, very close to the wording in [the 1981] article . . . which was obviously designed in the article to convey and elaborate upon the monofunctional approach." (Pet. at 38a). The court also found that "anyone reading the patent will find over and over again references which talk about the single terminal group." *Id.*

The court also rejected Dr. Jennings's testimony that the differences between his patent and his speech and article showed his intention to cover protein linkages

at both terminal ends of the polysaccharide (which results in crosslinking). The court found instead that:

> [T]here is nothing in this patent affirmatively teaching anything about achieving cross-linking. There is nothing in the patent except a negative view of cross-linking.

(Pet. at 40a). Thus, the court concluded that if Dr. Jennings intended to cover linkages at both terminal portions, "something that can be easily expressed in the English language," "[h]e did not express it." The court went on to explain:

> And that is the basic reason why I am holding in favor of the defendants on the question of interpretation. There are ample means through simple devices of wording to convey what he claims was his intention. He simply did not do it.

(Pet. at 39a).

In addition, the court rejected the testimony of Dr. Schoolnik for two independent reasons. First, Dr. Schoolnik's interpretation, focusing on the mention of *Haemophilus influenza* in claim 12, conflicted with the experiments and theory set forth in the patent. As the court explained:

> To allow all of that weight, really massive weight of discussion, descriptions of experiments and so forth, to be cancelled out by the two words "*Haemophilus influenza,*" in my mind, would not be a fair method of interpretation.

(Pet. at 41a). Second, the court recognized the illogic of Dr. Schoolnik's testimony that the mention of *Haemophilus influenza* in claim 12 "drives the interpretation of the entire patent" but the mention of polyfunctional polysaccharides in that same claim should be ignored

(Pet. at 40a). The court concluded that it would be "improper to ignore [the main teaching of the patent] in respect of *Haemophilus influenza* any more than for the [types of bacteria] where polyfunctionality occurs." (Pet. at 42a).

Thus, the district court concluded that the asserted claims were limited to conjugate vaccines with protein linked at one terminal portion of the polysaccharide. Since it was undisputed that a high proportion of Hib-TITER comprised conjugates with protein linked at both ends of the polysaccharide (i.e., were crosslinked), the court found no infringement and entered judgment for respondents.

The Appeal

On appeal, petitioners urged that claim construction in this case "is an issue of law freely reviewable on appeal" (29a). Respondents disagreed, but the Federal Circuit sided with petitioners and concluded that, under the particular facts of this case, claim interpretation "is a matter of law for this court to decide without special deference to the district court." (Pet. at 7a).

The Federal Circuit then began its analysis, as did the district court, "with the language of the claims themselves." (Pet. at 7a). The Federal Circuit focused first on the language "a terminal portion," noting that the claim could have used language expressly covering more than one terminal portion, and then looked to the patent for any indication "that the inventors here intended it to have other than its normal singular meaning." *Id.*

Like the district court, the Federal Circuit found no indication in the patent that the inventors intended to include crosslinking within the scope of their invention

(Pet. at 8a). To the contrary, the Federal Circuit observed that "[a]ll references to polysaccharide linkages speak of a linkage, not multiple linkages." *Id.* As one example, the Federal Circuit cited the same sentence from the patent's "summary of the invention" that the district court had cited and which appeared virtually verbatim in Dr. Jennings's article. *Id.*

The Federal Circuit also focused on Dr. Jennings's experiments reported in the examples of the patent, noting that these experiments also described the linkage in singular terms. In addition, the court cited one experiment where the conditions chosen were described as "unlikely" to produce linkage at both terminals. (Pet. at 9a). Thus, the Federal Circuit concluded that "[t]he examples in the [patent] specification also support linkage at only one terminal." (Pet. at 8a).

The Federal Circuit also addressed Dr. Jennings's testimony that he intended to include linkages at both ends of the polysaccharide within the scope of his invention. The Federal Circuit first explained that "[a] patent applicant cannot disclose and claim an invention narrowly and then, in the course of an infringement suit, argue effectively that the claims should be construed to cover that which is neither described nor enabled in the patent." (Pet. at 10a). The Federal Circuit then went on to rule Dr. Jennings's "after-the-fact testimony is of little weight compared to the clear import of the patent disclosure itself." *Id.*

As to Dr. Schoolnik's argument that the mention of *Haemophilus influenza* polysaccharide in claim 12 mandated an expansive interpretation of claim 11, the Federal Circuit rejected this contention on three grounds. First, it noted that dependent claims "are only an aid to

interpretation and are not conclusive" and could not dictate the interpretation of claim 11 in the absence of further disclosure of difunctional molecules in the patent (Pet. at 11a). Second, the Federal Circuit cited testimony from one of respondents' experts, Dr. Ronald Eby, that *Haemophilus influenza* could be treated to create a protein linkage at only one terminal portion of the polysaccharide. *Id.* Third, like the district court, it concluded that the interpretation of "linkage to a terminal portion" could not be dictated by claim 12 because polyfunctional polysaccharides, which petitioners conceded are not within the scope of the claimed invention, are also recited in claim 12. *Id.*

The Federal Circuit then commented on the district court's reliance on Dr. Jennings's speech and article. Apparently concerned that the district court had used the speech and article to interpret the claims rather than as an aid to understanding what was written in the patent and the testimony at trial (a concern that respondents believe was unwarranted), the Federal Circuit commented that "[a] patent is to be interpreted by what it states rather than by what the inventor wrote in a scientific publication." (Pet. at 13a). The Federal Circuit went to conclude that "it was error, albeit harmless error, for the district court to conclude that the narrow scope of the article limits the scope of the patent claims, which should be judged on their own merits." *Id.*

On the basis of the foregoing analysis, the Federal Circuit affirmed the district court's holding of noninfringement.

REASONS FOR DENYING THE WRIT

Petitioners' request for review by writ of certiorari of the Federal Circuit's decision should be denied because none of the requisite special and important reasons for review by this Court is presented. The Federal Circuit's decision raises none of the consideration set forth in Rule 10 of the rules of this Court. Moreover, several additional considerations, argued below, confirm that the petition should not be granted.

I.
PETITIONERS ARE ESTOPPED FROM ARGUING THAT THE FEDERAL CIRCUIT IMPROPERLY DECIDED CLAIM INTERPRETATION AS A MATTER OF LAW.

Before this Court, petitioners argue that the Federal Circuit "erred by deciding factual questions in interpreting the claims of the patent" and "intruded upon the assigned role of the District Court." Before the Federal Circuit, however, petitioners argued that claim interpretation in this case raised only "an issue of law" and asked the court to review the district court's claim construction "*de novo.*" Thus, if the Federal Circuit erred, petitioners, having invited the error, are estopped from asking this Court to review the Federal Circuit's interpretation of the claims.

At every opportunity before the Federal Circuit, petitioners argued that the claims should be interpreted as a matter of law. In their principal brief on appeal, petitioners argued "[c]laim construction is an issue of law freely reviewable on appeal" (29a). In their reply brief, petitioners argued "this appeal . . . raises only questions of law and does not involve disturbing any of the district court's underlying factual determinations" (30a). During

oral argument, and in response to questioning from the Federal Circuit panel as to whether the claim construction issue raised a question of law or fact, petitioners' counsel stated:

> We are not contesting any of the District Court's findings about any of those terms . . . the question before this Court is one of claim construction that should be reviewed *de novo,* Your Honor.

(32a).

The Federal Circuit adopted petitioners' argument, holding that resolution of the disputed issues "regarding the meaning of contested language . . . is a matter of law for this court to decide without special deference to the district court." (Pet. at 7a). The Federal Circuit proceeded to interpret the claims, committing what petitioners now allege to be error.

Having repeatedly invited the Federal Circuit to construe the claims "as a matter of law," petitioners complain now that the Federal Circuit erred by doing just that. A party cannot appeal, however, from an alleged error induced by its own action. *See, e.g., F.W. Woolworth Co. v. Contemporary Arts, Inc.,* 344 U.S. 228, 231 (1952) (no right to complain of exclusion of evidence in response to petitioner's own objections); *Perego v. Dodge,* 163 U.S. 160, 164-65 (1896) (no right to complain that a complaint in equity should have been dismissed because of an adequate remedy at law when the petitioner voluntarily invoked equity jurisdiction); *St. Louis Public Schools v. Risley,* 77 U.S. 91 (1870) (no right to predicate error on instructions given at petitioner's own request). Moreover, after waiving a position before the Court of Appeals, an appellant cannot resurrect that position before this Court. *See Helvering v.*

Wood, 309 U.S. 344, 349 (1940) (petitioner not permitted to raise an issue which he had expressly waived in his brief before the Circuit Court of Appeals).

Thus, in view of their argument urged upon and adopted by the Federal Circuit, petitioners are estopped from reversing their position and arguing now that the Federal Circuit erred by interpreting the claims as a matter of law.

II.
THE FEDERAL CIRCUIT DID NOT ENGAGE IN FACT FINDING.

The Federal Circuit did not "improperly [decide] the disputed facts underlying the interpretation of the patent claims" as petitioners allege. The Federal Circuit's opinion is premised upon the language of the claims and the disclosure in the patent. Beyond that, the Federal Circuit rejected petitioners' testimonial evidence on legal grounds. Thus, the Federal Circuit properly interpreted the claims as a matter of law.

Like the district court, the starting point for the Federal Circuit's analysis was the claim language. The Federal Circuit properly viewed itself as capable of understanding the English language. In so doing, the Federal Circuit agreed with the district court's understanding that the language "a terminal portion," standing alone, means a single terminal portion.

The Federal Circuit then looked to the disclosures in the patent, finding many references to linkages to a single terminal portion of the polysaccharide, no affirmative teaching of linking protein to both terminal portions of the polysaccharide, and a clear teaching away from cross-linking. Thus, like the district court, the Federal Circuit

concluded that the description of the invention in the patent suggested that the scope was limited to conjugates with protein linked to a single terminal portion of the polysaccharides.

The Federal Circuit then addressed petitioners' arguments in favor of a more expansive interpretation of the claims – Dr. Jennings's testimony as to his intended meaning of the patent's disclosure and claims, and Dr. Schoolnik's testimony as to the import of claim 12 mentioning *Haemophilus influenza* polysaccharide. The Federal Circuit rejected Dr. Jennings's testimony on legal grounds – intent of the inventor is irrelevant to claim interpretation. The Federal Circuit then rejected Dr. Schoolnik's testimony on multiple grounds, including his inability to explain why mention of *Haemophilus influenza* polysaccharide in claim 12 should mandate the interpretation of claim 11 while other polysaccharides should be ignored. The district court rejected Dr. Schoolnik's testimony for similar reasons.

Thus, the second reason given by the Federal Circuit for rejecting Dr. Schoolnik's testimony, the testimony by Dr. Eby establishing that Hib polysaccharide can be pretreated such that protein will link to only one terminal portion of the polysaccharide, was unnecessary to its analysis. Petitioners misrepresent the record, however, when they argue that the Federal Circuit relied on testimony that "contradicts a finding of the District Court" and assert that "[t]he District Court specifically stated that it would not rely upon the testimony of this witness in interpreting the patent . . . ." (Pet. at 12). Dr. Eby's testimony was fully consistent with the district court's opinion. Indeed, the district court cited a related stipulation that "on some of these [types of bacteria] which would not naturally and easily yield the monofunctional

result, such a result could be obtained if there was pretreatment of the kind taught at an earlier point in the patent." (Pet. at 41a). Moreover, the district court never suggested that it would not rely on any of Dr. Eby's testimony, only that it would not rely on Dr. Eby's "opinion on interpretation" (28a).

In short, following the Federal Circuit's analysis, no outstanding factual disputes remained to be tried. As a result, the Federal Circuit properly construed the claims as a matter of law.

III.
THE DISTRICT COURT'S JUDGMENT WAS NOT SUBSTANTIALLY INFLUENCED BY THE ALLEGED ERROR.

The district court's judgment was not "substantially influenced" by the alleged error. With or without Dr. Jennings's speech and article, the district court almost certainly would have adopted the same claim interpretation.

A careful review of the district court opinion reveals that the district court reached its claim interpretation principally because (1) the phrase "linkage to a terminal portion of the polysaccharide" ordinarily would be viewed as meaning a single linkage ("[t]he phrase 'a terminal [portion]', of course, is in the singular" Pet. at 38a); (2) the patent described the linkage only in singular terms ("anyone reading the patent will find over and over again references which talk about the single terminal group," *Id.*); and (3) the patent described only the absence of crosslinking ("[t]here is nothing in the patent except a negative view of crosslinking," Pet. at 40a). The speech and article had little bearing on any of these three elements of the district court's analysis.

Thus, contrary to petitioners' allegations, the article and speech were not "the basic reason" the district court ruled in favor of respondents or "the most important point in the evidence" for the district court. (See Pet. at 8). The "basic reason" given by the district court for ruling in defendant's favor was:

> There are ample means through simple devices of wording to convey what [Dr. Jennings] claims was his intention. He simply did not do it.

(Pet. at 39a). In other words, the patent disclosed no support for petitioners' claim interpretation. Furthermore, the "most important point in the evidence" was Dr. Jennings's monofunctional objective in "the laboratory work . . . leading up to the patent." (Pet. at 35a). That objective was manifested throughout the patent itself, especially in the examples of the patent which described exactly the same experiments that had been reported earlier in the speech and article.

The district court used the speech and article principally to evaluate Dr. Jennings's testimony that he "intended" his invention to cover protein linkages at both ends of the polysaccharide and that he "expressed" that intention in the patent. The district court disagreed, recognizing that the patent described the same experiments and used the same language appearing in Dr. Jennings's speech and article, which Dr. Jennings unequivocally admitted were directed toward a monofunctional approach. Thus, the district court used the speech and article for what respondents believe was an entirely proper purpose – to help it understand the *disclosures* in the patent, not as a basis for construing the *claims* per se as the Federal Circuit seemed to suggest.

Even if the district court's reliance on Dr. Jennings's speech and article was error, however, its judgment was not swayed by the error. As noted above, the district court relied principally upon the claim language and the patent disclosure, both of which the district court viewed, standing alone, as supporting the claim interpretation adopted. Beyond that, the district court addressed the testimony of Dr. Jennings and Dr. Schoolnik that the claim should be interpreted more broadly, neither of which would have been bolstered by ignoring the speech and article.

Dr. Jennings's testimony was impeached by the speech and article, but the Federal Circuit ruled that Dr. Jennings's testimony was "of little weight" in any event, a ruling not challenged by petitioners. Thus, his testimony cannot be grounds for concluding that the district court might have reached a different result without the speech and article. Indeed, without his testimony, there would have been little need for the district court to rely on the speech and article.

The district court's rejection of Dr. Schoolnik's testimony was not dependent upon the speech and article. Dr. Schoolnik's testimony centered on his argument that the interpretation of the patent should be driven by the mention of *Haemophilus influenza* polysaccharide in claim 12. The district court rejected this testimony, however, because Dr. Schoolnik could offer no explanation as to why the Hib polysaccharide should dictate the meaning of claim 11 while other polysaccharides, incompatible with his claim interpretation, should be ignored. This analysis of his testimony was completely unrelated to the district court's consideration of Dr. Jennings's speech and article.

Thus, even without the speech and article, there can be little doubt that the district court would have reached the same conclusion. Notwithstanding the district court's polite remarks at the beginning of its opinion, this was not a "close" case. Given the district court's analysis and the Federal Circuit's ruling regarding the testimony of Dr. Jennings, virtually no record evidence supports petitioners' strained interpretation of the claims.

In short, this is a case like *United States v. Borden Co.*, 347 U.S. 514 (1954), a Sherman Act case where this Court, after considering the record and the offers of proof, held that certain evidentiary rulings, even if error, were harmless, explaining:

> it does not appear that admission of the evidence in question would have been sufficient to change the conclusion that the Government had not established a case under the Sherman Act; hence the rulings cannot be said to have affected substantial rights of the parties within the meaning of 28 U.S.C. §2111.

Id. at 516. Similarly here, because it is unlikely that the Federal Circuit's evidentiary ruling would have changed the district court's interpretation of the claim language, the district court's reliance on that evidence did not affect the substantial rights of petitioners within the meaning of 28 U.S.C. §2111. Thus, the Federal Circuit properly affirmed the district court judgment.

Finally, the application of the harmless error doctrine was peculiar to the facts and proceedings in this case. Consequently, the Supreme Court's review of this case would be of little value to future cases. As this Court observed in *Kotteakos v. United States*, 328 U.S. 750 (1946):

> In the final analysis judgment in each case must be influenced by conviction resulting from examina-

> tion of the proceedings in their entirety, tempered but not governed in any rigid sense of stare decisis by what has been done in similar situations.

Id. at 762. Thus, this petition does not warrant certiorari.

CONCLUSION

For the foregoing reasons, the petition for a writ of certiorari should be denied.

Respectfully submitted,

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APPENDIX A – United States Patent 4,356,170
columns 2, 3 and 10

IMMUMNOGENIC POLYSACCHARIDE-PROTEIN CONJUGATES

Salmonella O-antigens: preparation of an octasaccharide-bovine serum albumin immunogen representative of Salmonella sero-group B O-antigen and characterization of the antibody response", J. of Immunol. 120, 1750, 1978. References (4), (5) and (7) used water-soluble carbodiimide reagents and formed amido linkages to the protein. Reference (6) carried out a more complex procedure including activation of the polysaccharide with cynaogen bromide, first conjugation of the protein with adipic hydrazide, then treating the mixture with a water-soluble carbodiimide; to form an amido type linkage to the protein and a complex variety of linkages from the adipic spacer to the polysaccharide. These previous methods either (a) utilized many randomly activated functional groups (hydroxyl or carboxylate) on the various polysaccharides leading to considerable crosslinking and poorly defined, low solubility conjugates; (b) required a specific functionality of limited applicability; (c) resulted in less incorporation of polysaccharide than was desired; or (d) led to extraneous modification of the polysaccharide which would alter its antigenicity.

Relatively small disaccharides have been conjugated to protein via their terminal hemiacetal groups using sodium cyanoborohydride reagent. See: (8) B. A.

Schwartz and G.R. Gray, Arch. Biochem. Biophys. 181, 542-49, 1977. When we attempted to apply this technique to the high molecular weight meningococcal polysaccharides, unsatisfactory incorporation resulted.

SUMMARY OF THE INVENTION

We have found it possible to introduce a free aldehyde group into the polysaccharide molecule in a terminal location and to specifically couple this aldehyde group to protein without activating other functional groups on the polysaccharide. This procedure avoids crosslinking and extraneous chemical modification of the bulk of the polysaccharide resulting in better defined immunogens.

This invention includes a method of preparing antigenic polysaccharide: Protein conjugates, comprising:

(a) providing an antigenic polysaccharide which has reactive vicinal hydroxyl groups in a terminal portion of the molecule;

(b) subjecting said vicinal hydroxyl groups at a terminal location to controlled oxidation to generate a reactive aldehyde group therefrom on the polysaccharide;

(c) selecting a physiologically tolerated protein having a free amino group and reacting said amino group with said aldehyde group by reductive amination, to covalently link said polysaccharide and protein; and

(d) recovering a substantially non-crosslinked, soluble, antigenic polysaccharide:protein conjugate.

Another part of the invention is the antigenic-polysaccharide:protein conjugate wherein the polysaccharide and protein are covalently linked through a

$$-CH_2-\underset{\text{H}}{N}-\text{protein}$$

linkage to a terminal portion of the polysaccharide without significant cross-linking, said antigenic polysaccharide having a MW above about 2000.

The invention further includes a vaccine comprising at least one of said conjugates, particularly a vaccine for human infants, and a method of immunizing with said vaccines.

DETAILED DESCRIPTION

Various antigenic polysaccharides may be used according to this invention, the only requirement being that they contain vicinal hydroxyl groups in a terminal portion of the molecule. In particular, capsular polysaccharides from bacteria are most suitable for vaccine purposes. In some cases, unlinked terminal non-reducing sialic acid residues are present in the polysaccharide and they contain suitable vicinal hydroxyl groups. Polysaccharides which initially have a terminal reducing sugar residue can be subjected to a controlled reduction to generate reactive vicinal hydroxyl groups from this terminal residue. One particular example of such a reducing sugar residue is the N-acetylmannosamine residue. Other samples of such residues include those of glucose, glucosamine, rhamnose, and ribose. Antigenic polysaccharides which are particularly useful include those derived from meningococci, *Haemophilus influenza,* pneumococci, *B*-hemolytic streptococci and *Escherichia coli.* The polysaccharide MW suitably is within about 2,000-100,000 for best coupling and antigenicity.

The reduction of the terminal reducing sugar residues is suitably effected using a mild reducing agent, e.g.

sodium borohydride or its equivalent at a pH of about 7.5 to 10. Preferably $NaBH_4$ is used at a pH of 8-9 to minimize side reactions.

It has been found possible to selectively oxidize the terminal vicinal hydroxyl groups to form a terminal aldehyde group by controlled oxidation. This oxidation may be effected conveniently with periodate reagent for a limited time. For instance, approximately 10 mg of polysaccharide suitably is oxidized with about 1 ml of approximately 100 mM sodium metaperiodate solution for about 10-15 min. at room temperature. The reaction time can be varied to accomodate other amounts of periodate to obtain equivalent oxidation. The vicinal hydroxyl groups are cleaved to leave the terminal —CHO group on the polysaccharide.

The protein component may be any physiologically tolerated protein having a free amino group. Preferably, the protein is itself an immunogen. Suitable proteins include tetanus toxoid, diphtheria toxoid and other proteins derived from vacteria. It is possible that other proteins containing lysine residues, e.g. a synthetic polylysine may be useful in a particular system. The bacterial source may be, e.g. *B*-hemolytic streptococci, *Haemophilus influenza,* meningococci, pneumococci and *E. coli.* If desired, both polysaccharide and protein can be derived from the same bacteria to give a stronger immunogenic effect. The toxoids of tetanus and diphtheria have been approved for human use, and tetanus toxoid was used in the examples. However, other proteins would be operative.

The reductive amination covalently couples the terminal aldehyde group of the polysaccharide to a free amino group on the protein through a

$$-CH_2-\underset{\displaystyle H}{N}-\text{protein}$$

linkage where the $-CH_2-$ derives from the aldehyde group. There is no significant cross-linking by this method and the conjugates are water-soluble to a considerable extent. A cyanoborohydride reagent may be utilized to effect this reductive amination. The amount of cyanoborohydride is not critical. Typical amounts may range from about 30 to 100% by wt. based on the

* * *

17. The conjugate of claim 16 wherein said reducing sugar moiety is N-acetylmannosaminitol.

18. The conjugate of claim 11 wherein said linkage is through a lysine amino group on the protein.

19. The conjugate of claim 11 wherein the polysaccharide and protein are derived from the same bacteria.

20. A method of immunizing against infection susceptible humans or animals comprising, administering a vaccine comprising the conjugate of claim 11 in an immunogenic amount by intramuscular or subcutaneous injection.

21. The method of claim 20 wherein the dosage of the conjugate is equivalent to from about 5 to about 25 micrograms for the human infant.

22. The method of claim 21 wherein human infants are immunized with a vaccine comprising at least one of (a) the conjugate of meningococcal polysaccharide, and (b) the conjugate of *H. influenza* polysaccharide.

23. A vaccine comprising at least one conjugate as defined in claim 11.

24. A vaccine for infants comprising the conjugate of claim 11 wherein the initial non-conjugated polysaccharide is of the type for which the immune response is non-thymus-controlled.

25. A human infant vaccine comprising the conjugate of claim 11 wherein the polysaccharide comprises at least one of meningococcal polysaccharide and *Haemophilus influenza* polysaccharide.

26. A vaccine as in claim 24 in a dosage unit form wherein the conjugate is present in the equivalent of from about 5 to about 25 micrograms based on the human infant.

* * * * *

APPENDIX B – Excerpts from trial transcripts of Northern American Vaccine, Inc. and National Research Council of Canada v. American Cyanamid Company and Praxis Biologics, Inc. (United States District Court for the Southern District of New York in 91-CV-1449) (1992)

John Diaz, Esquire Opening Statement (August 3, 1992)

[12] so when it did make antibodies to one of these highly cross-linked or significantly cross-linked conjugates, it made antibodies to these proteins but those antibodies were not effective against that was causing the infection which in this case is the polysacchride.

So this system did not work because it was too heavy, it sunk the ship, molecules came out of the solution and in addition the proteins masked the polysacchride so that the immune system could not see it and would not make effective antibodies. And that was the problem that the '170 patent addresses and that is the problem that the '170 patent solves and it solves it as you've just seen by just making polysacchride chains which have free aldehyde groups, single terminal aldehyde groups on one end or on both ends and leaves this backbone clean.

If we could put that PX 306, maybe put that on the second easel. Your Honor, if you contrast 306 to 302, the significant differences are the backbone in 306, the backbone of the patented conjugate molecules is clean as a whistle. That's significant. When that molecule is injected into the human body, human infant system, the human infant immune system sees the polysacchride, if that's Haemophilus influenza it sees that and it makes antibodies to it. If it's mening, it sees the mening and makes antibodies to it. It cannot do that with these highly

* * *

Dr. Gary Schoolnik Cross-Examination
(August 10, 1992)

[539] be read a terminal aldehyde group at each end.

Now, let me just concede something to you. If the Haemophilus influenzae polysaccharide was not mentioned in that claim, and if it were not the subject of this suit, I would be far more comfortable, perhaps, being persuaded by your argument. But for me, you know – I'm speaking only as an expert witness here, I guess – the fact that that polysaccharide is mentioned specifically in the claim, the fact that those skilled in the art as of 1981 knew its structure and knew what would happen to it upon periodate oxidation, I interpret all of this language with reference to that, and that's just, you know, how I have come to understand these words.

Q. Is it your view, Dr. Schoolnik, that because certain polysaccharides are mentioned in the claims, that based on what would happen to those polysaccharides in this periodate oxidation reaction, you have to modify this phrase accordingly, namely, that's how you find out what a terminal aldehyde group means? Is that your view?

A. My view is that since we are really talking about the Haemophilus influenzae polysaccharide, and in reference in particular to that polysaccharide and this lang uage, my view is that this language is interpretable for me – now I'm just saying for me as a scientist, I would go to the claims, and since Hib polysaccharide is what we're all

[540] talking about here, I would say how does this language read with respect to what we know about Hib or what we would have known about it as of 1981.

Now, all of the other polysaccharides that are present in that claim may or may not be relevant. But for me as a scientist, since we are talking about a specific example, I'm not that concerned about the other polysac-

charides there. I am concerned about Hib and how we would interpret this language with respect to it.

Q. But if you're interpreting this language with respect to Hib, when you look at claim 12, you also have to interpret the language with respect to the other polysaccharides that are mentioned there, isn't that right, by pure logic?

A. Well, we've made, I think, a general agreement over the last several days of testimony that one must, as a matter of principle, interpret the language with respect to each of the polysaccharides that might come under consideration. So, I mean, I suppose if this was a suit about pneumococcal vaccine, then we would spend most of our time wondering about the pneumococcal polysaccharide and how the language would pertain to it.

Q. But I'm asking you, I mean, we are not restricted to any specific word in this claim. In claim 12, is it not true that there's a group of polysaccharides which include

[541] meningococci, Haemophilus influenza, pneumococci, B-hemolytic streptococci, and E. coli? Does it include all of those?

A. Well, it does.

Q. Just yes or no. Does it include them?

A. Yes.

Q. Please restrict yourself to answering my questions.

A. Yes, it does.

Q. Now, if you are interpreting this language you just read in column 3 with respect to Haemophilus influenza, doesn't pure logic – you told me you studied logic – doesn't pure logic tell you that you also have to look to the other polysaccharides by the same token and in the same manner?

A. Well, we could go over each one of them and see. But I tell you to me, as a scientist, where I have to deal with reactions as they occur on a particular molecule, I

try to be as focused in my comments as possible.

Now, maybe that's not what a good lawyer would do, but as a scientist, I am concerned with the examples in the patent. And we've talked extensively about those, and I'm concerned about only one of that group, namely, Haemophilus influenza, because that's what's at suit.

Beyond that, you know, I would have to put on my

[542] scientist hat and reanalyze the relevance of each of the many other – you know, we have quite a few polysaccharides listed there. I would have –

THE COURT: They're all referred to. I'll tell you, you're not the lawyer, you don't have to worry about what the case is about or the issues in the case. Obviously you're a very sophisticated man. You're not coming in here and acting like a robot. You want to know the context and the purpose of your testimony, and of course you know what the case is about. But it really is not up to you to argue the case, it's to simply testify.

And every single of one of those diseases, becteria, whatever you call them, are listed in 12, and they're all relevant. Regardless of what this case is about, they're relevant to the interpretation of the patent, and that's what Mr. Dunner simply asked you.

And I think the answer is yes. If you're interpreting the patent, if you're interpreting claim 12, you have to take into account everything in claim 12, right? You do?

THE WITNESS: All right. I –

THE COURT: Of course you do.

THE WITNESS: Okay.

THE COURT: Let me just interrupt, and you can go back to your train of questions, but if you could just take

* * *

[596] THE WITNESS: That's correct.

THE COURT: Okay.

MR. DUNNER: And, your Honor, my point is merely that he keyed everything to whether it's antigenic or not.

THE COURT: No, he didn't.

THE WITNESS: Part of it is simply starting with your proposition you come out with a dirty backbone.

MR. DUNNER: Which he defined as something which was not antigenic.

THE COURT: Well, okay.

Q. Is that correct?

THE COURT: I guess there will be other things that could make things antigenic. If it was just, you know, skimmed milk it wouldn't be antigenic either.

Q. To proceed, Dr. Schoolnik, you also are of the view that, to the extent pneumococci serotypes have dirty backbones, they would not be included within these claims, correct, not be embraced by them?

A. It just seems to me that –

Q. Yes or no?

THE COURT: Please, that's sort of a yes or no question. The answer is yes, isn't it?

THE WITNESS: Yes.

Q. And that's also true of every B-hemolytic streptococci, correct, the same thing?

[597] A. Yes.

Q. The same thing is true about E. coli?

A. Yes.

Q. Well, let's just examine some of these structures. I'd like you to look at exhibit K, if you would, in your book. That is an article written by Dr. Jennings, is it not?

A. Yes.

Q. I'd like you to look at page 105 of this paper and page 106, 106 in particular.

A. All right.

Q. Toward the bottom you will see –

MR. DIAZ: Your Honor, I'm just going to offer a formal objection, technical objection on this article. The patent speaks as of the time it was filed, May 1981. He's talking about a 1990 article.

THE COURT: This article is what?

MR. DIAZ: It's a 1990 article.

THE COURT: Well, I don't know whether it bears or not. We'll just have to see.

MR. DIAZ: I just want to register a formal objection.

THE COURT: Overruled. We will take it for whatever weight it is worth. If it is not entitled to weight, I will not give it any.

* * *

Dr. Gary Schoolnik Cross-Examination
(August 11, 1992)

[766] Cynamid memorandum entitled the Jennings '170 patent describes forming a single aldehyde group at one end of a polysaccharide, that is the title of the memorandum. And it is dated August 5, 1992. So that's what my question is about.

And the question is: In light of those quotations from the patent which really do speak of a terminal or a terminally-located aldehyde through – all in the singular, and we've been through those quotations many times in the trial, I'd like to get your position as to why, in view of those, why this patent can be interpreted as covering the formation of the polysaccharide protein conjugate, and I'll use it in the best sense I can, with aldehydes at both terminal ends?

THE WITNESS: Well, my position is that although

this uses the singular, my position is that the singular refers to one end of a molecule that may have more ends, two or more ends. It's not inconsistent with a single terminal aldehyde on each of the two ends. And my reasons for that come, by and large, from the fact that within the claims, and in specific, claim 12, there are several examples, including Haemophilus influenza, which if one practiced the art and one knew, and having knowledge of the structures of these polysaccharides as of 1981, one would anticipate the production of aldehydes at both ends as well as in some

[767] cases one end.

So my entire interpretation of the language where it is singular is driven by the specific examples of polysaccharides in claim 12, which because of their structural properties, when subjected to oxidation, would yield a polysaccharide molecule with an aldehyde at both ends. So that for me is the most compelling reason, okay.

THE COURT: Now, I would also – I don't know whether – maybe this is not feasible for you, but, again, taking advantage of your presence here, I want to ask you something and it relates to a memorandum filed by Cynamid today, and you would have no reason to have read this, but I have.

Now, let me ask you this, are you now familiar with what I think the lawyers have called the prior art, and what I assume that to mean is that the experimentation, the developments, the successes, the failures of this field of technology prior to the Jennings patent?

THE WITNESS: I believe I am.

THE COURT: All right, now. Would you take – I should have given this to you before the recess, but we can just sit here for a minute now. Would you read the portion of this memorandum at the bottom of page 2

underneath the heading which starts with, Dr. Jennings's role, and would you read it going over to – read that paragraph. Now, the

* * *

Dr. Harold J. Jennings Direct-Examination
(August 17, 1992)

[957]won't bother getting it out because there is no dispute about that.

Did you testify in deposition in words or substance that you gave your 1980 article, PX-168, to your patent attorney and he used that article as a basis for drafting your patent application.

A. Yes.

THE COURT: Is this '80 or '81?

MR. DIAZ: It's the '81 article.

THE COURT: Was this based on an '80 talk?

MR. DIAZ: Based upon the '80 talk, you Honor.

Let me see if I can clarify the record.

Q. The '81 article, Exhibit 168, is kind of a summation or, it has in substance what you presented orally at the 1980 NIH symposium, is that correct?

A. It's practically identical, and I gave the patent attorney the draft of the 1981 paper, the experimental part, to write the patent.

Q. So PX-168 had not been published and you gave him a draft of that publication?

A. Yes, I did.

Q. Would you please turn to Plaintiff's Exhibit 168, page 1016. And about right-hand column, about lines 15 to 17. Do you see that, where you state – why don't you read that beginning with "The ideal situation."

* * *

[965]THE COURT: Look, I'm not criticizing, you have a right to read and you generally don't read, but anyway, if you read, just go a little slower, because I'm trying to make notes.

MR. DIAZ: You're right, I would prefer not to read. With the Court's indulgence, I will try not to read.

Q. I'm talking about your 1981 and 1982 articles, I've read them, you've read them.

And when I read them, they talk about experiments which are carried out on specific polysaccharides, and the specific polysaccharides in those articles are mening A, mening B, and mening C, correct?

A. Correct.

THE COURT: Just a minute.

(Pause)

THE COURT: Go ahead.

Q. When you gave your 1981 article in manuscript form to your patent attorney, did you tell your patent attorney that he should restrict the application in your invention to mening A, B, and C?

A. No.

Q. Did you discuss with your patent attorney whether your conjugates should be restricted to conjugates in which the polysaccharide component was mening A, mening B, and/or mening C?

[966]A. I discussed with the patent attorney the general applicability of the method to other important polysaccharides, and I believe these other important polysaccharides are mentioned in the patent. They are Haemophilus influenza, streptococcus pneumonia, group B streptococcus, and Escherichia coli.

Q. Did your patent attorney agree with you or disagree with you when you told him you wanted to include these other polysaccharides?

A. He was very positive about including these.

Q. And did he include these other polysaccharides?

A. Yes, he did.

Q. So that when you wrote your patent application, you considered your invention to be broader than the specific experiments you had carried out as of that date, i.e., experiments with mening A, mening B and mening C, right?

A. Yes, I did.

Q. And you put that into your patent application, did you not?

A. I did.

Q. Would you look please at the patent which is in your book as PX-10; and I'm directing your attention to column 3, line 18-20.

Are the polysaccharides which you've just

* * *

[984]Would you mark that mening C?

A. Yes (complying).

Q. Thank you.

(Witness resumed the stand)

Q. Now, Doctor Jennings, it is defendants' contention in this case that in the experiment on Group C reported in Columns 5 and 6 of your patent, you intentionally selected starting materials and conditions so as to achieve a monofunctional Group C polysaccharide chain. Is that contention correct?

A. That's not correct.

Q. When you started off planning your Group C experiment, what result did you expect to achieve?

A. Well, I suppose, in effect, we would be willing to accept any result, as long as we could get terminal aldehydes. I mean, we didn't really care.

Q. Right.

A. And in actual fact, what we got, in essence, was an aldehyde at one end.

Q. And did you expect to get an aldehyde at both ends?

A. We would have anticipated that we would, yes.

Q. And that anticipation was based upon your 1975 work with mening C; is that correct?

A. Yes.

* * *

[1000] about 2,000."

Q. My specific question is: In the terminology you use there "linkage to a terminal portion of the polysaccharide," by that statement did you intend that the linkage of protein had to be to only one terminal portion of the polysaccharide?

A. No, we did not.

Q. Would you look, please, at claim 11, and it's up on the board here, where that same language is used, "linkage to a terminal portion of the polysaccharide." Do you see that?

By that language, did you intend that the linkage had to be to one terminal portion of the polysaccharide?

A. No.

Q. Did you intend in that language to be broad enough to include linkage to both ends of the polysaccharide?

A. What we intended it to be, also to cover the aldehyde at each end, and this can be read from the difference between my publications and also the abstract — sorry, the patent, in which we do allow for cross-linking.

Now, to get cross-linking, we would have to have at least two aldehydes on one polysaccharide molecule.

Q. To get some cross-linking you would have to have two aldehydes, one on each end?

* * *

Dr. Harold J. Jennings Cross-Examination (August 17, 1992)

[1107] Q. And you could have done it and you didn't do it?

A. That's correct.

Q. And the results of your consultation with Connaught, no product according to the Jennings method, right?

A. According to my method, they did make a product.

Q. What product did they make?

A. They sent me details of a conjugate that they made and I looked at the results that they got and I wrote back to them and told them how to make this a better type of conjugate.

Q. They sent you an experimental batch of conjugate that they had made according to your procedure, meningococcal conjugate, right?

A. But they also sent me the written work that describes this conjugate.

Q. With regard to the meningococcal conjugate, correct?

A. That's correct.

Q. And you got it and you reviewed it and you talked to them about it some more, right?

A. That's correct.

Q. And what I'm saying is when all is said and done, they never took that, they never developed it they never tried to license it and they never marketed it in the United

[1108] States or anywhere, correct?

A. That's correct.

Q. And the fact of the matter is that Connaught does make a conjugate vaccine, don't they?

A. Yes, they do.

Q. They make a conjugate vaccine against Hib, correct?

A. That's correct.

Q. And they do not use the Jennings method?

A. That's correct.

Q. Indeed they use the Robbins and Schneerson method, correct?

A. I think they use a derivation of it, but not exactly the Robbins and Schneerson method.

Q. Well, if you looked at the package insert, you would see the footnotes of Robbins and Schneerson up front?

A. That's true, basically.

Q. The basic underlying principle for the Connaught vaccine was Robbins and Schneerson?

A. That's correct.

Q. And they make it and it works in two-, four- and six-month olds.

A. That's not correct.

Q. It doesn't work in two-, four- and six-month olds?

[1109] A. Not the first vaccine that they made, no.

Q. Well, they make one today that works in two-, four-, and six-month olds?

A. I'm sorry, I'm confused by – I thought you were talking about the first one that they made.

Q. Let's talk about today. Connaught makes a Hib vaccine, it's a conjugate vaccine and it works, correct?

A. This is the one that is supplied through the Institute Mirieux. I've heard of it, I've heard that they're doing it.

Q. You're a man in this field, are you interested when somebody succeeds in putting on together a conjugate vaccine that you've been working on for over a decade?

A. Yes, I am interested.

Q. That captures your attention?

A. Yes. But, on the other hand, I do not know the exact procedure that they're using now because I have no relationship with Connaught anymore.

Q. I understand, but you are aware and you know

that they use a derivation of the Schneerson and Robbins method to make a Hib vaccine and that vaccine works in infants, doesn't it?

A. Yes, it does.

Q. There is absolutely no proof that the Jennings method, when applied to any polysaccharide, can yield a

* * *

[1134] Q. And that describes the conjugates that you had actually made in your lab, right?

A. That's correct.

THE COURT: What exhibit is this?

MR. THOMASCH: This is Plaintiff's Exhibit 168, your Honor.

THE COURT: That's the '81 article?

MR. THOMASCH: The '81 article given to Mr. Thomson.

Q. Regardless of the similarities or differences between this article and the patent, the experimental work which underlies this article is the very same experiments that are reported on in the patent, correct?

A. That's correct.

Q. All right. Now I'd like to take a look at your language in this article that you drafted, and start at page 1012. The article begins, "Despite the demonstrated success of the groups A and C capsular polysaccharides of Neisseria meningitidis in providing homologous serogroup immunity in humans, there still remain major problems associated with their use as human vaccines."

That is verbatim the same introduction that you gave to the NIH, correct?

A. Yes.

Q. And what you are saying here is that the capsular

* * *

Dr. Ronald John Eby Direct-Examination
(August 19, 1992)

[1323] A. Approximately a third of the articles and all the of the abstracts.

Q. Dr. Eby, I want to go back in time. When did you start working for Praxis?

A. I started in October of 1983.

Q. What was your initial position?

A. I was hired as a research scientist.

Q. What were your initial responsibilities as a research scientist?

A. I was hired to develop the Haemophilus B conjugate vaccine for Praxis.

Q. Could you slow down again?

A. Yes, I could.

Q. When you started working for Praxis, where did you work specifically?

A. Initially, I worked in the laboratory of Porter Anderson at the University of Rochester.

Q. Did Praxis have laboratory space available for you in its facilities at the time?

A. Not at that time. They were undergoing construction of those facilities.

Q. Approximately what number hire were you at Praxis? How many people we are employed by Praxis before you got there?

A. I was approximately number six in the employees.

[1324] Q. Through what period of time did you work in Dr. Anderson's laboratory?

A. Approximately from October of 1983 through January of 1984.

Q. When did you first meet Dr. Anderson?

A. I met Dr. Anderson in a job interview in August of 1983.

THE COURT: You worked for Anderson at Praxis, right?

THE WITNESS: I worked with Dr. Anderson.

THE COURT: At Praxis?

THE WITNESS: Yes. Praxis at that time existed at 300 East River Road, but there was no lab facilities available, so for the interim I was using the facilities at the University of Rochester.

Q. You mentioned that during a job interview you talked with Dr. Anderson. During that job interview, did you discuss polysaccharide protein conjugates?

A. Yes. We have discussed the work that Dr. Anderson had performed on preparing oligosaccharide Haemophilus conjugates, link to proteins. His work on use of the acid hydrolysis and reductive amination of those oligosaccharides to the protein.

We discussed their immunogenicity in terms of both animals and humans, and we continued to discuss other

[1325] of preparing conjugate vaccines of Haemophilus, and, in particular, we discussed the use of periodate oxidation to generate fragments and to couple those fragments to proteins to make conjugate vaccines.

Q. During the job interview while you were talking with Dr. Anderson, did you discuss any advantages of periodate cleavage approach?

A. Yes. We looked at the chemistry, we looked at the structure of the Haemophilus polysaccharide, determined where cleavage sites would occur in the polysaccharide that reaction of those vicinal hydroxyl groups in the molecule would lead to the formation of fragments, that these fragments would indeed have aldehydes at both ends of the fragments, that we could control the reaction by the amount of periodate used in the reaction and the oxidation step.

We discussed the difference that these fragments would have free aldehydes over what he had currently been

using in the acid hydrolysis step, and that there would be a difference in reactivity of these aldehydes which would lead to an increase yield in the reaction.

We also discussed a little bit of the possible type of conjugates that we would form, that we would have fragments which would have two aldehydes, and therefore, we would have the potential of crosslinking occurring in the conjugates.

[1326] Q. When you were hired by Praxis, what was your understanding of the first work that you would be doing for Praxis?

A. Well, based on the extensive job interview, it was my idea that I would be working on the formation of the Haemophilus B conjugate vaccine using the periodate approach.

Q. Was that what actually happened?

A. Yes, it was.

Q. When you started working for Praxis, what was your understanding of the general business plan of Praxis?

A. Well, the general business plan was to first commercialize the polysaccharide vaccine to develop the manufacturing capability, to sell that product which would be the polysaccharide vaccine.

Q. When you speak of the term polysaccharide vaccine, are you speaking of the polysaccharide from Hib as its purified from the bacteria?

A. Yes.

Q. It was not a conjugate vaccine?

A. That's right. The initial products Praxis had envisioned was the Haemophilus polysaccharide for Haemophilus B disease, and that was our primary goal. We would use the sale of the polysaccharide vaccine to generate revenue that would continue to drive the research of the

* * *

[1336] age, infants?

A. Approximately one year later we had an approval for 15 months and older.

Q. Did Praxis ultimately get approval for infants at two, four, and six months, for its HibTITER vaccine?

A. After the successful completion of an efficacy trial in northern California, which indicated that the vaccine had a 100 percent efficacy in the young infant, we were granted a license for the infant indication. I believe that was in October of 1990.

Q. Dr. Eby, what competitors of Lederle Praxis sell vaccines for Hib in the United States?

A. There are two competitors. One is Merck and the other is Merieux Connaught.

Q. With respect to Merieux Connaught, what is the name and type of the vaccine that they sell?

A. They sell Haemophilus B conjugate vaccine called Prohibit which basically is a vaccine prepared by the method of Schneerson and Robbins.

Q. For what age groups is Prohibit approved?

A. Currently Prohibit is approved for infants 15 months and older.

Q. That's in the United States?

A. That's in the United States.

Q. Is Prohibit approved for infants anywhere in the

* * *

[1338] months of age.

Q. What is the market share tha the Merck product has in the market for Hib vaccines in the U.S.?

A. Currently, the Merck product occupies about 5 percent of the market.

Q. Does that mean that HibTITER has about 88 percent of the market for Hib vaccines in the U.S. today?

A. That's correct.

Q. How long has HibTITER had such a large market share?

A. The product was granted an infant license in 1990 and we got about that market share several months, one or two months, after that licensure.

Q. Are you aware of any reports dealing with the incidence of meningitis caused by Hib since HibTITER started being marketed?

A. Yes, I am.

Q. What do those reports conclude?

A. Those reports conclude that there has been a marked decease in the incidence of Haemophilus disease after licensure of the conjugate vaccines in infants.

Q. Is that decrease due to the sales of HibTITER?

A. Primarily due to the sales of HibTITER, since we currently have about 88 percent of the market.

Q. Dr. Eby, we'll be putting up on the easel a copy

* * *

[1344] native polysaccharide, that we have shown at the top of this exhibit, that the periodate cleavage could occur anytime, or any location where there is vicinal hydroxyls which occurs repeatedly along the length of the polysaccharide chain?

A. Exactly. Again, we're not confined to just where the yellow arrows are, but anyplace we have vicinal hydroxyl groups, anywhere along the polysaccharide chain, you can get cleavage with periodate.

Q. The brackets show with subscripts various numbers, 20, 40, 10 and 30. Does that denote that within the brackets there would be various numbers of repeating units?

A. Yes, this is just a shorthand way of saying that these repeating units within this bracket are repeated 20 times, that the repeating units inside this bracket are

repeated 40 times. It's just a random way of showing that this is a very long molecule and instead of taking up the whole courtroom, we've reduced it down to a poster size board in which we have fragments or brackets with different sizes in polysaccharide.

Q. Would you now describe what happens when you treat the starting Hib polysaccharide with periodate in the process for making HibTITER?

A. When the Haemophilus B polysaccharide in the native state is treated with periodate which is denoted by

[1345] the IO4 minus, that is the periodate ion, there undergoes a random cleavage in the backbone between the vicinal hydroxyl groups of the ribotol unit to give you fragments of random molecular size with aldehyde functions at each end of the fragment. So there is cleavage between the vicinal hydroxyl groups and for formation of aldehyde groups at each end of the fragment. And what is denoted in the schematic is that we can generate fragments having aldehydes at both ends but also fragments of various sizes so that we can get a random mixture of fragments, sizes anywhere from very small to very large, all of which will have aldehyde groups at both ends of the molecule.

(Continued on next page)

* * *

[1348] Q. Would you describe what's illustrated on exhibit XH?

A. On exhibit XH is a schematic of the overall production of the Haemophilus B conjugate vaccine known as HibTITER from the starting polysaccharide all the way through the conjugation reaction.

What we saw in the previous exhibit was basically

the top portion of this schematic in which now the polysaccharide is denoted by this long wavy line on the left-hand side of the schematic. We removed all of the chemistry, essentially, that we saw in the previous exhibit.

That polysaccharide undergoes a random oxidative cleavage with periodate to generate smaller fragments having aldehydes at both ends of the fragments. These fragments, as we pointed out before, are sized to a narrow-size distribution, not shown in this particular schematic.

These fragments are then coupled to a protein denoted by the circle in the diagram, and in particular, in Hib-TITER, this protein is CRM 197. The protein is coupled to the fragments by a process called reductive amination in which the aldehyde groups are reacted with the amino groups on the protein to give us a conjugate vaccine, denoted in the bottom row of the schematic.

Q. You mentioned that the protein was CRM 197?

A. Uh-huh.

* * *

[1351] appears to be attached in two different ways, one at one end and one polysaccharide is attached at both ends to the same protein. What do you call that when the polysaccharide is attached at both ends to the same protein?

A. Again, because we are using fragments which have aldehydes at both ends, both ends of the molecule are reactive. They can attach themselves to one side to the protein and what we call a loop and attach themselves to the other side of a protein molecule. So this formation where the fragment is linked at both ends to the same protein molecule, this is called a loop structure.

Q. Would you also point out on the exhibit the existence of crosslinking?

A. Okay. Crosslinking occurs when you have structures higher than monomer, in other words, dimers, trimers, any fragments that may even be higher than that. That occurs when the saccharide binds at one end to one protein molecule and the other end binds to another protein molecule, not the same protein.

So if the fragment binds to the same protein molecule, you get a loop; if it binds to two different protein molecules, you get a crosslink between them.

Q. Dr. Eby, what is the estimated molecular weight of a typical monomer structure in HibTITER?

A. Typically, the protein is approximately 60,000.

* * *

Dr. Ronald John Eby
Cross-Examination (August 20, 1992)

[1447] simply referring to different parts of the patent about which I had heard many times.

And so I will say right now that on the question of interpretation, his opinion on interpretation, I really will disregard that testimony. Not any disrespect to you, but we had those objections and it was repetitious anyway, and so you do not need to cross-examine him about that and try to undermine his opinion about interpretation because he really didn't give anything very much.

Let's move on.

MR. DIAZ: Okay, I understand the Court will not rely upon that testimony in interpreting the patent.

THE COURT: Yes, right.

MR. DIAZ: Thank you very much, your Honor.

Q. At pages 23 and 24, defendants' pretrial memorandum –

THE COURT: All right, now let me get that.

(Continued on the next page)

* * *

APPENDIX C – Excerpt from Brief of Plaintiffs-Appellants North American Vaccine, Inc. and National Research Council of Canada filed at the United States Court of Appeals for the Federal Circuit on January 15, 1993

Claim construction is an issue of law freely reviewable on appeal. *Stiftung v. Renishaw PLC*, 945 F.2d 1173, 1177, 20 USPQ2d 1094, 1097 (Fed. Cir. 1991); *Specialty Composites v. Cabot Corp.*, 845 F.2d 981, 986, 6 USPQ2d 1601, 1604 (Fed. Cir. 1988); *Intervet America, Inc. v. Kee-Vet Laboratories, Inc.*, 887 F.2d 1050, 1053, 12 USPQ2d 1474, 1476 (Fed. Cir. 1989).

Here, the claim language and the specification require a construction of the claims to embrace *Haemophilus influenza* polysaccharides with a protein linkage to both terminal portions. The claims expressly recite *Haemophilus influenza* polysaccharides and the specification expressly teaches the use of *Haemophilus influenza* polysaccharides in the invention. Since *Haemophilus influenza* polysaccharides are the only polysaccharides present in Cyanamid's HibTITER product and they include a protein linkage to both terminal portions, infringement follows as a matter of law.

A. The Claim Language "*Haemophilus Influenza*" Requires That The Claims Be Interpreted To Include, Not Exclude, *Haemophilus Influenza* Polysaccharides With A Protein Linkage To Both Terminal Portions

"Claim interpretation must begin with the language of the claim itself." *Stiftung*, 945 F.2d at 1177, 20 USPQ2d at 1098. The express recitation of *Haemophilus influenza* in the claims requires that "a terminal portion" be

APPENDIX D – Excerpt from Reply Brief from Plaintiffs-Appellants North American Vaccine, Inc. and National Research Council of Canada filed at the United States Court of Appeals for the Federal Circuit on April 15, 1993

ARGUMENT

I. THE DISTRICT COURT'S JUDGMENT OF NONINFRINGEMENT SHOULD BE REVERSED AS A MATTER OF LAW.

Contrary to the impression that Cyanamid seeks to create with its brief, NRC's position in this appeal calling for reversal of the district court's judgment of noninfringement raises only questions of law and does not involve disturbing any of the district court's underlying factual determinations.

The first step in the infringement analysis is claim interpretation which is a question of law as shown in NRC's main brief and as developed further in this reply brief. The second step in the infringement analysis, application of the properly interpreted claims to the accused product, involves no factual issues in this case because the composition of the accused HibTITER product is undisputed.

A. Cyanamid Cannot Defend The District Court's "Monofunctional" Claim Construction Which Erroneously Excluded "Difunctional" *Haemophilus Influenza* Polysaccharides From The Claims

Cyanamid's attempt to posture the appeal as involving fact issues, subject to the clearly erroneous standard of review, cannot withstand analysis. At the heart of this

appeal is the district court's construction of asserted claims 12 and 25 as limited to what it called "mono-functionality," *i.e.*, protein linkage to *only*

APPENDIX E – Excerpt from transcript of Oral Argument at the United States Court of Appeals for the Federal Circuit on July 12, 1993

Judge: There at least two hotly contested terms as I have heard the argument this morning . . .

Smith: Right . . .

Judge: And you've just given me . . .

Smith: If you take that claim language, and it's the interplay between that claim language and the recitation of Haemophilus influenza in the claim which has the linkage to both ends, and the interplay between all those factors adds up to the ball of wax that is called claim construction, that is the province of this court to review de novo. We are not contesting any of the District Court's findings about any of those terms, we are flowing with that, the question before this Court is one of claim construction that should be reviewed de novo, Your Honor.

Judge: Thank you, Mr. Smith.

Smith: Thank you very much.

Judge: Case is submitted.

(3)

No. 93-1385

Supreme Court, U.S.
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IN THE
Supreme Court of the United States
OCTOBER TERM, 1993

NORTH AMERICAN VACCINE, INC., and
NATIONAL RESEARCH COUNCIL OF CANADA,
Petitioners,

v.

AMERICAN CYANAMID COMPANY and
PRAXIS BIOLOGICS, INC.,
Respondents.

On Petition for a Writ of Certiorari to the United States Court of Appeals for the Federal Circuit

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PETITIONERS' REPLY BRIEF

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---

PETITIONERS' REPLY BRIEF

INTRODUCTION

The Federal Circuit's affirmance of the judgment of noninfringement on "harmless error" grounds despite its rejection of the "basic reason" for the District Court's decision calls into question the fundamental relationship between the Federal Circuit and the United States District Courts in deciding patent cases. Although determining that "it was error . . . for the district court to conclude that the narrow scope of the article limits the scope of the patent claims," Pet. App. at 13a, the Federal Circuit did not remand. Instead, the Federal Circuit took it upon itself to determine the teachings of the patent disclosure and the meaning of technical terms in the claims, both of which are disputed questions of fact. Respondents' ac-

knowledgement that the Federal Circuit "viewed itself as capable of understanding the English language" of the patent crystallizes the procedural issue raised by this Petition. Opposition at 16.

The Federal Circuit made its findings without the benefit of having sat through a three-week trial, as the District Court did, in which five scientific witnesess gave testimony as to what the patent means to one skilled in the art. Respondents demonstrate the Federal Circuit's error in substituting its judgment for that of the District Court by devoting a substantial portion of their brief and appendix to the extensive testimony adduced at trial. *E.g.*, Opposition at 5-8, 17-20; Resp. App. at 12a-28a.

The issue raised by this Petition is not, as Respondents urge, "peculiar" to this case. Opposition at 21. Most patent cases involve similar questions of fact regarding the meaning of technical terms in patent claims and the teachings of patent disclosures. Because the Federal Circuit is the only Court of Appeals in the federal judicial system having jurisdiction over appeals from District Courts in patent cases, this Court should grant the Petition in order to clarify the Federal Circuit's appellate role.

I. BOTH THE FEDERAL CIRCUIT AND RESPONDENTS HAVE MISAPPLIED THE HARMLESS ERROR DOCTRINE

Respondents' basic position is that the District Court's error was harmless because it would have reached the same result even if it had not improperly relied on the inventor's article and speech. Opposition at 18, 21. Respondents engage in speculation when they purport to divine what the District Court would have done had it not erroneously relied on the article and speech. The proper standard is not "whether there was enough to support the result" but whether the District Court's judgment was "substantially swayed" or "influence[d]" by the error. *Kotteakos* v. *United States,* 328 U.S. 750, 765 (1946).

It could not be clearer that the District Court was "substantially swayed" and "influenced" by the article and speech in reaching its judgment of noninfringement. Containing no less than 33 references to the "article" and "speech," the District Court opinion reveals that those documents were at the heart of the District Judge's thought process. For example, the District Court stated: "[T]he most important point in the evidence" was the inventor's laboratory work as "made clear in his National Institute of Health speech and in the article he wrote in 1981," Pet. App. at 35a-36a; "the summary of the invention in the patent . . . is very, very close to the wording in that article," *id.* at 38a; "the concept of the speech and article was carried over into the patent," *id.* at 39a; and "the basic reason why I am holding in favor of the defendants on the question of interpretation" is that the inventor did not clearly express in the patent a desire to "broaden his patent beyond what was contained in the article and the speech," *id.* at 39a.

Respondents' suggestion that the District Court "relied principally on the claim language and the patent disclosure . . . standing alone" in finding noninfringement, Opposition at 20, is contradicted by the District Court itself. During trial the District Court clearly indicated that it very well might have reached the opposite result based on the wording of the patent alone:

> Look, if I just read the patent and I had nothing to do but stare at the language of the patent, I would find it a little difficult to give tremendous significance to the use of the singular rather than the plural. I think a person could talk about creating this linkage at a terminal end, and if some one created it at two terminal ends, they are in a sense doing it at a terminal end and then they're doing it again at a terminal end. And so there would be a pretty good argument that they have infringed the patent.

Tr. at 1622, Aug. 24, 1992.

In its opinion, the District Court similarly found:

> Now, as I've said many times during the trial, we cannot solve this problem by staring at the language and simply saying there is a singular indefinite article and a singular noun and that is that. It is perfectly possible, as an initial proposition, that the phrase "a terminal portion" is a generic term and could mean exactly what plaintiffs say it means.
>
> In order to solve the problem, we need to look at some of the other evidence that can be considered properly under the law on the question of interpretation.

Pet. App. at 34a.

After considering the large volume of highly technical evidence in the record, the District Court went out of its way to note that "the case is a close one." Pet. App. at 29a. Respondents assert that the District was simply being polite when it said this. However, in view of the Court's comments set forth above and its further statement that "the scales tip, not drastically, but I think they tip in favor of the defense," *id.* at 29a, the District Court obviously regarded the case as a close one.

It is the province of the District Court, not the Federal Circuit, to weigh the evidence, and it is manifestly inappropriate to apply the harmless error doctrine to a "close" case where the District Court's decision so clearly turned upon error.

II. RESPONDENTS' ARGUMENTS DEMONSTRATE THAT THE FEDERAL CIRCUIT IMPROPERLY ENGAGED IN FACT FINDING

Respondents argue that the Federal Circuit did not engage in fact finding because its "opinion is premised upon the language of the claims and the disclosure in the patent." Opposition at 16. They assert that "[t]he Federal Circuit properly viewed itself as capable of un-

derstanding the English language" and "looked to the disclosures in the patent, finding . . . no affirmative teaching of linking protein to both terminal portions . . . and a clear teaching away from crosslinking." *Id.* However, "what a patent teaches is fact finding, not interpretation." *Panduit Corp.* v. *Dennison Mfg. Co.*, 810 F.2d 1561, 1579 n.42 (Fed. Cir.), *cert. denied*, 481 U.S. 1052 (1987). The Federal Circuit must review such findings of fact under the "clearly erroneous" standard. *See Dennison Mfg. Co.* v. *Panduit Corp.*, 475 U.S. 809, 810-11 (1986).

A patent is a technical document whose teachings are to be interpreted through the eyes of a person skilled in the art, not a judge or lay person. *Carnegie Steel Co.* v. *Cambria Iron Co.*, 185 U.S. 403, 437-38, 441 (1902) ("[t]he specification of the patent is not addressed to lawyers, or even to the public generally" but "to those engaged and skilled in the art"); *Biodex Corp.* v. *Lorendan Biomedical, Inc.*, 946 F.2d 850, 862 (Fed. Cir. 1991), *cert. denied*, 112 S.Ct. 2957 (1992) ("claims are drafted to be read by those skilled in the art, rather than lay persons"); *Moeller* v. *Ionetics, Inc.*, 794 F.2d 653, 657 (Fed. Cir. 1986) ("the test of claim interpretation is directed to one skilled in the art").

The Federal Circuit is in no position to resolve disputes as to the meaning of technical terms in a claim or as to what a patent teaches to one skilled in the art. *See Webster Loom Co.* v. *Higgins*, 105 U.S. (15 Otto) 580, 585-86 (1882) ("as it cannot be expected that the court will possess the requisite knowledge [of a person of ordinary skill in the art], it becomes necessary that it should avail itself of the light furnished by the evidence to enable it to understand the terms used in the patent and the devices and operations described or alluded to therein.").

Here, the meaning of the patent claims and disclosure are questions of fact because they contain technical terms ("*Haemophilus* influenza") and "terms of art" ("linked . . . to a terminal of the polysaccharide" and "without

significant crosslinking") as to which "the testimony of scientific witnesses is indispensable." *Seymour* v. *Osborn*, 78 U.S. (11 Wall.) 516, 546 (1871). Indeed, the meaning of those terms was the central dispute at trial. Pet. App. at 30a, 2a, 5a. Thus, "resolution of factual issues as a basis for interpretation of the claim" was required. *H.H. Robertson Co.* v. *United Steel Deck, Inc.*, 820 F.2d 384, 389 (Fed. Cir. 1987). Indeed, the District Court expressly stated that extrinsic evidence was required to resolve the meaning of the disputed claim language. Pet. App. at 34a.

Not only did the Federal Circuit overstep its reviewing function by making fact findings as to technical terms and teachings of the patent, it did so by improperly usurping the District Court's role to weigh the trial testimony. The Federal Circuit credited some trial testimony and rejected or ignored other trial testimony. *Id.* at 10a. ("Dr. Jennings . . . testimony is of little weight"); *id.* at 11a (crediting testimony of Dr. Eby); *id.* at 4a-14a (not addressing the testimony of Dr. Schoolnik on infringement).

Respondents acknowledge that "the Federal Circuit rejected petitioners' testimonial evidence," but erroneously argue that the Federal Circuit did so "on legal grounds." Opposition at 16. Respondents' assertion that the Federal Circuit rejected Dr. Jennings' testimony as legally irrelevant is belied by the Federal Circuit's statement that his testimony was entitled to "little weight." Their assertion that the Federal Circuit rejected Dr. Schoolnik's testimony because of "his inability to explain" his interpretation of the claims amply demonstrates that the Federal Circuit was improperly making a credibility determination. Opposition at 17.

Finally, Petitioners' statement that the Federal Circuit's reliance on testimony of Dr. Eby is contrary to a critical fact finding of the District Court and the District Court's assessment of Dr. Eby's testimony was not a misrepresentation. Opposition at 18. The Federal Circuit relied on

Dr. Eby's testimony that *Haemophilus* influenza b can be made monofunctional, Pet. App. at 11a, whereas the District Court found *Haemophilus* influenza b "yields the difunctional result," *id.* at 41a.

The Federal Circuit is simply not empowered to weigh witness credibility, and its piecemeal, selective review of testimony was improper.

III. THE PETITION IS CONSISTENT WITH PETITIONERS' ARGUMENTS TO THE FEDERAL CIRCUIT

Respondents incorrectly argue that the position now taken by Petitioners in seeking certiorari is inconsistent with the position they took before the Federal Circuit. Petitioners seek certiorari because the Federal Circuit engaged in *de novo* fact finding as to the teachings of the patent disclosure and the meaning of disputed technical terms in the claims. Before the Federal Circuit, however, Petitioners argued that reversal follows as a matter of law from the District Court's fact findings.[1] At no time did Petitioners ask the Federal Circuit either to set aside the fact findings of the District Court or engage in its own fact finding. To the contrary, Petitioners urged that the ultimate question of claim construction "does not involve disturbing any of the district court's underlying factual determinations." Opposition at 14.

Respondent are wrong in asserting that Petitioners "invited the error" by the Federal Circuit. The Federal Circuit was well aware that "a genuine evidentiary conflict underlying the meaning of claim terms raises a question of fact." Pet. App. at 7a.

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[1] Petitioners argued that because (a) the patent claims and disclosure expressly include *Haemophilus* influenza, and (b) the District Court found that *Haemophilus* influenza b has protein linkages to both terminal portions of the polysaccharide, *i.e.*, "yields the difunctional result", Pet. App. at 41a, the claim must be construed as a matter of law to cover difunctionality. Appellants' Main Brief at 8-12 and Appellants' Reply Brief at 1-4.

However, the Federal Circuit appears to have carved out an exception to the "clearly erroneous" constraint on its power of review where the "questions . . . go to the heart of what the claims mean," stating: "It is a matter of law for this court to decide without special deference to the district court." *Id.* No such distinction can be made because all disputed claim terms affect the meaning of the claims and what they cover. Here, three weeks of trial testimony were directed to the meaning of the disputed claim terms in light of the teachings of the patent disclosure. Only the District Court was in a position to evaluate this evidence properly.

CONCLUSION

For the foregoing reasons and the reasons set forth in the Petition, Petitioners respectfully request that their Petition for a Writ of Certiorari be granted.

Respectfully submitted,

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